(12) INTERNATIONAL APPLICATION PUBLISHED UNDER THE PATENT COOPERATION TREATY (PCT)

(19) World Intellectual Property Organization
International Bureau

(43) International Publication Date
27 March 2003 (27.03.2003)

PCT

(10) International Publication Number
WO 03/024923 A1

(51) International Patent Classification⁷: C07C 311/45, C07D 295/215, 215/48, 277/42, 417/12, 213/82, 213/81, 209/08, 295/155, A61K 31/18, 31/27, 31/496, 31/47, 31/5375, 31/426

(21) International Application Number: PCT/US02/28505

(22) International Filing Date: 9 September 2002 (09.09.2002)

(25) Filing Language: English

(26) Publication Language: English

(30) Priority Data:
60/322,220 14 September 2001 (14.09.2001) US

(71) Applicant *(for all designated States except US)*: **AXYS PHARMACEUTICALS, INC.** [US/US]; 180 Kimball Way, South San Francisco, Ca 94080 (US).

(72) Inventor; and
(75) Inventor/Applicant *(for US only)*: **PALMER, James** [US/US]; 131 Koch Road, Corte Madera, CA 94925 (US).

(74) Agents: BANSAL, Rekha et al.; Celera Genomics, 180 Kimball Way, South San Francisco, CA 94080 (US).

(81) Designated States *(national)*: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW.

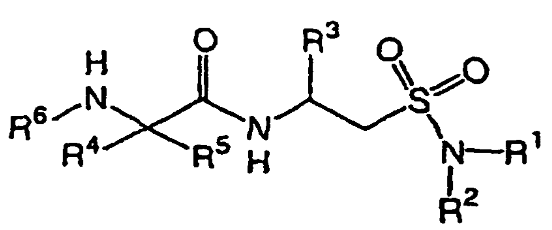
(84) Designated States *(regional)*: ARIPO patent (GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW), Eurasian patent (AM, AZ, BY, KG, KZ, MD, RU, TJ, TM), European patent (AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, SK, TR), OAPI patent (BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG).

Published:
— *with international search report*

For two-letter codes and other abbreviations, refer to the "Guidance Notes on Codes and Abbreviations" appearing at the beginning of each regular issue of the PCT Gazette.

WO 03/024923 A1

(54) Title: SULFONAMIDE COMPOUNDS AS PROTEASE INHIBITORS



(I)

(57) Abstract: The present invention relates to cysteine protease inhibitors of the general formula I, the pharmaceutically acceptable salts and *N*-oxides thereof; their uses as therapeutic agents and the methods of their making.

SULFONAMIDE COMPOUNDS AS PROTEASE INHIBITORS

BACKGROUND OF THE INVENTION

Field of the Invention

This application relates to compounds and compositions for treating diseases associated with cysteine protease activity, particularly diseases associated with activity of cathepsins B, K, L or S.

State of the Art

Cysteine proteases represent a class of peptidases characterized by the presence of a cysteine residue in the catalytic site of the enzyme. Cysteine proteases are associated with the normal degradation and processing of proteins. The aberrant activity of cysteine proteases, e.g., as a result of increased expression or enhanced activation, however, may have pathological consequences. In this regard, certain cysteine proteases are associated with a number of disease states, including arthritis, muscular dystrophy, inflammation, tumor invasion, glomerulonephritis, malaria, periodontal disease, metachromatic leukodystrophy and others. For example, increased cathepsin B levels and redistribution of the enzyme are found in tumors; thus, suggesting a role for the enzyme in tumor invasion and metastasis. In addition, aberrant cathepsin B activity is implicated in such disease states as rheumatoid arthritis, osteo arthritis, pneumocystis carinii, acute pancreatitis, inflammatory airway disease and bone and joint disorders.

The prominent expression of cathepsin K in osteoclasts and osteoclast-related multinucleated cells and its high collagenolytic activity suggest that the enzyme is involved in ososteoclast-mediated bone resorption and, hence, in bone abnormalities such as occurs in osteoporosis. In addition, cathepsin K expression in the lung and its elastinolytic activity suggest that the enzyme plays a role in pulmonary disorders as well.

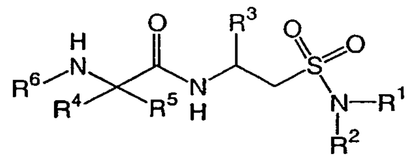
Cathepsin L is implicated in normal lysosomal proteolysis as well as several disease states, including, but not limited to, metastasis of melanomas. Cathepsin S is implicated in Alzheimer's disease and certain autoimmune disorders, including, but not limited to juvenile onset diabetes, multiple sclerosis, pemphigus vulgaris, Graves' disease, myasthenia gravis, systemic lupus erythemotasus, rheumatoid arthritis and Hashimoto's thyroiditis. In addition, cathepsin S is implicated in: allergic disorders, including, but not limited to asthma; and allogeneic immune reponses, including, but not limited to, rejection of organ transplants or

tissue grafts.

In view of the number of diseases wherein it is recognized that an increase in cysteine protease activity contributes to the pathology and/or symptomatology of the disease, molecules which are shown to inhibit the activity of this class of enzymes, in particular molecules which are inhibitors of cathepsins B, K, L and/or S, will be useful as therapeutic agents.

SUMMARY OF THE INVENTION

In one aspect, this invention is directed to a compound of Formula I:



I

in which:

R^1 and R^2 independently are $-R^8$, $-X^2OR^8$, $-X^2SR^8$, $-X^2S(O)R^8$, $-X^2S(O)_2R^8$, $-X^2C(O)R^8$, $-X^2C(OR^7)R^7R^8$, $-X^2C(O)OR^8$, $-X^2NR^7R^8$, $-X^2NR^7C(O)OR^8$, $-X^2C(O)NR^7R^8$, $-X^2S(O)_2NR^7R^8$, $-X^2NR^7C(O)NR^7R^8$ or $-X^2NR^7C(NR^7)NR^7R^8$, wherein X^2 is (C_{1-6})alkylene, R^7 is hydrogen or (C_{1-6})alkyl; R^8 is hydrogen, (C_{1-6})alkyl, (C_{3-12})cycloalkyl(C_{0-3})alkyl, hetero(C_{5-12})cycloalkyl(C_{0-3})alkyl, (C_{6-12})aryl(C_{0-3})alkyl, hetero(C_{5-12})aryl(C_{0-3})alkyl, (C_{9-12})bicycloaryl(C_{0-3})alkyl or hetero(C_{8-12})bicyclo-aryl(C_{0-3})alkyl; wherein within R^8 said cycloalkyl, heterocycloalkyl, aryl, heteroaryl, bicycloaryl or heterobicycloaryl ring may be substituted with halo, $-R^9$, $-X^3OR^9$, $-X^3SR^9$, $-X^3S(O)R^9$, $-X^3S(O)_2R^9$, $-X^3C(O)R^9$, $-X^3C(OR^9)R^9$, $-X^3C(O)OR^9$, $-X^3NR^9R^{10}$, $-X^3NR^9C(O)OR^9$, $-X^3C(O)NR^9R^{10}$, $-X^3S(O)_2NR^9R^{10}$, $-X^3NR^9C(O)NR^9R^{10}$ or $-X^3NR^9C(NR^9)NR^9R^{10}$; wherein X^3 is a bond or (C_{1-6})alkylene, R^9 is hydrogen or (C_{1-6})alkyl and R^{10} is cycloalkyl;

R^3 is $-R^{11}$, $-X^3OR^{11}$, $-X^3SR^{11}$, $-X^3S(O)R^{11}$, $-X^3S(O)_2R^{11}$, $-X^3C(O)R^{11}$, $-X^3C(O)OR^{11}$, $-X^3NR^{11}R^{12}$, $-X^3NR^{12}C(O)OR^{11}$, $-X^3C(O)NR^{11}R^{12}$, $-X^3S(O)_2NR^{11}R^{12}$, $-X^3NR^{12}C(O)NR^{11}R^{12}$ or $-X^3NR^{12}C(NR^{12})NR^{11}R^{12}$, wherein X^3 is as described above, R^{11} is hydrogen, (C_{1-6})alkyl, halo(C_{1-6})alkyl, (C_{3-12})cycloalkyl(C_{0-3})alkyl, hetero(C_{5-12})cycloalkyl-(C_{0-3})alkyl, (C_{6-12})aryl(C_{0-3})alkyl, hetero(C_{5-12})aryl(C_{0-3})alkyl, (C_{9-12})bicycloaryl(C_{0-3})alkyl or hetero(C_{8-12})bicycloaryl(C_{0-3})alkyl and R^{12} is hydrogen or (C_{1-6})alkyl, wherein any 1 to 3 annular atoms of any aromatic ring with available valences comprising R^3 are optionally independently substituted with halo, nitro, cyano, (C_{1-6})alkyl, halo-substituted(C_{1-6})alkyl, $-OR^7$,

$-C(O)R^7$, $-C(O)OR^7$, $-C(O)NR^7R^7$, $-S(O)_2NR^7R^7$, $-X^2NR^7R^7$, $-X^2NR^7C(O)OR^7$, $-X^2NR^7C(O)NR^7R^7$ or $-X^2NR^7C(NR^7NR^7R^7$, wherein X^2 and $R^7$are as defined above;

R^4 is hydrogen or (C_{1-6})alkyl;

R^5 is (C_{1-6})alkyl, halo(C_{1-6})alkyl, (C_{3-12})cycloalkyl(C_{0-3})alkyl, or $-X^2S(O)R^{14}$ where X^2 is as defined above and R^{14} is (C_{3-12})cycloalkyl(C_{0-3})alkyl, hetero(C_{5-12})cycloalkyl(C_{0-3})alkyl, (C_{6-12})aryl(C_{0-3})alkyl, hetero(C_{5-12})aryl(C_{0-3})alkyl, (C_{9-12})bicycloaryl(C_{0-3})alkyl or hetero(C_{8-12})bicycloaryl(C_{0-3})alkyl; or R^4 and R^5 together with the carbon atom to which R^4 and R^5 are attached form (C_{3-7})cycloalkylene;

R^6 is hydrogen or $-X^4X^5R^{13}$, wherein X^4 is -C(O)-, X^5 is a bond, -O- or $-NR^{12}-$, wherein R^{12} is as defined above, and R^{13} is (C_{1-6})alkyl, $-R^{14}$, $-X^3OR^{14}$, $-X^3SR^{14}$, $-X^3S(O)R^{14}$, $-X^3S(O)_2R^{14}$, $-X^3C(O)R^{14}$, $-X^3C(O)OR^{14}$, $-X^3NR^{14}R^{15}$, $-X^3NR^{15}C(O)OR^{14}$, $-X^3C(O)NR^{14}R^{15}$, $-X^3S(O)_2NR^{14}R^{15}$, $-X^3NR^{15}C(O)NR^{14}R^{15}$ or $-X^3NR^{15}C(NR^{15})NR^{14}R^{15}$, wherein X^3 is as defined above; R^{14} is (C_{3-12})cycloalkyl(C_{0-3})alkyl, hetero(C_{5-12})cycloalkyl(C_{0-3})alkyl, (C_{6-12})aryl(C_{0-3})alkyl, hetero(C_{5-12})aryl(C_{0-3})alkyl, (C_{9-12})bicycloaryl(C_{0-3})alkyl or hetero(C_{8-12})bicycloaryl(C_{0-3})alkyl; R^{15} is hydrogen or (C_{1-6})alkyl; and within R^{14} said cycloalkyl, heterocycloalkyl, aryl, heteroaryl, bicycloaryl or heterobicycloaryl ring may be substituted with $-OCF_3$, $-CF_3$, -OH, halo, $-R^{16}$, $-X^3OR^{16}$, $-X^3OR^{15}$, $-X^3C(O)R^{15}$, $-X^3SR^{16}$, $-X^3S(O)R^{16}$, $-R^{15}$, $-X^3S(O)_2R^{16}$, $-X^3C(O)R^{16}$, $-X^3C(O)OR^{15}$, $-X^3NR^{15}R^{15}$, $-X^3NR^{15}C(O)OR^{15}$, $-X^3C(O)NR^{15}R^{16}$, $-X^3S(O)_2NR^{15}R^{16}$, $-X^3NR^{15}C(O)NR^{15}R^{15}$ or $-X^3NR^{15}C(NR^{15})NR^{15}R^{16}$, wherein X^3 and R^{15} are as defined above and R^{16} is (C_{3-12})cycloalkyl(C_{0-3})alkyl, hetero(C_{5-12})cycloalkyl(C_{0-3})alkyl, (C_{6-12})aryl(C_{0-3})alkyl, hetero(C_{5-12})aryl(C_{0-3})alkyl, (C_{9-12})bicycloaryl(C_{0-3})alkyl or hetero(C_{8-12})bicycloaryl-(C_{0-3})alkyl and within R^{16} said cycloalkyl, heterocycloalkyl, aryl, heteroaryl, bicycloaryl or heterobicycloaryl ring may be substituted with $-R^{15}$, $-R^{17}$, $-X^3OR^{17}$, $-X^3SR^{17}$, $-X^3S(O)R^{17}$, $-X^3S(O)_2R^{17}$, $-X^3C(O)R^{17}$, $-X^3C(O)OR^{17}$, $-X^3NR^{15}R^{17}$, $-X^3NR^{15}R^{15}$, $-X^3NR^{15}C(O)OR^{17}$, $-X^3C(O)NR^{15}R^{17}$, $-X^3S(O)_2NR^{15}R^{17}$, $-X^3NR^{15}C(O)NR^{15}R^{17}$ or $-X^3NR^{15}C(NR^{15})NR^{15}R^{17}$, wherein X^3 and R^{15} are as defined above and R^{17} is (C_{3-12})cycloalkyl(C_{0-3})alkyl, hetero(C_{5-12})cycloalkyl(C_{0-3})alkyl, (C_{6-12})aryl(C_{0-3})alkyl, hetero(C_{5-12})aryl(C_{0-3})alkyl, (C_{9-12})bicycloaryl(C_{0-3})alkyl or hetero(C_{8-12})bicycloaryl(C_{0-3})alkyl and within R^{17} said cycloalkyl, heterocycloalkyl, aryl, heteroaryl, bicycloaryl or heterobicycloaryl ring may be substituted with $-R^{18}$, $-X^3OR^{18}$, $-X^3SR^{18}$, $-X^3S(O)R^{18}$, $-X^3S(O)_2R^{18}$, $-X^3C(O)R^{18}$, $-X^3C(O)OR^{18}$, $-X^3NR^{15}R^{18}$, $-X^3NR^{15}C(O)OR^{18}$, $-X^3C(O)NR^{15}R^{18}$, $-X^3S(O)_2NR^{15}R^{18}$, $-X^3NR^{15}C(O)NR^{15}R^{18}$ or $-X^3NR^{15}C(NR^{15})NR^{15}R^{18}$, wherein X^3 and R^{15} are

as defined above and R^{18} is (C_{3-12})cycloalkyl(C_{0-3})alkyl, hetero(C_{5-12})cycloalkyl(C_{0-3})alkyl, (C_{6-12})aryl(C_{0-3})alkyl, hetero(C_{5-12})aryl(C_{0-3})alkyl, (C_{9-12})bicycloaryl(C_{0-3})alkyl or hetero(C_{8-12})bicycloaryl(C_{0-3})alkyl; with the proviso that only one (C_{9-12})bicycloaryl(C_{0-3})alkyl or hetero(C_{8-12})bicycloaryl(C_{0-3})alkyl is present within R^6, or

a pharmaceutically acceptable salt thereof.

A second aspect of this invention is a pharmaceutical composition that contains a compound of Formula I or a pharmaceutically acceptable salt thereof in admixture with one or more suitable excipients.

A third aspect of this invention is a method of treating a disease in an animal in which inhibition of a cysteine protease can prevent, inhibit or ameliorate the pathology and/or symptomatology of the disease. Said method comprises administering to the animal a therapeutically effective amount of compound of Formula I or a pharmaceutically acceptable salt thereof.

A fourth aspect of this invention is the processes for preparing compounds of Formula I and the pharmaceutically acceptable salts thereof as set forth in "Detailed Description of the Invention".

DETAILED DESCRIPTION OF THE INVENTION

Definitions:

Unless otherwise stated, the following terms used in the specification and claims are defined for the purposes of this Application and have the meanings given this Section:

"Aliphatic" means a moiety characterized by straight or branched chain arrangement of the constituent carbon atoms and may be saturated or partially unsaturated with two or more double or triple bonds.

"Alkyl" represented by itself means a straight or branched, saturated or unsaturated, aliphatic radical having the number of carbon atoms indicated (e.g., (C_{1-6})alkyl includes methyl, ethyl, propyl, isopropyl, butyl, *sec*-butyl, isobutyl, *tert*-butyl, vinyl, allyl, 1-propenyl, isopropenyl, 1-butenyl, 2-butenyl, 3-butenyl, 2-methylallyl, ethynyl, 1-propynyl, 2-propynyl, and the like). Alkyl represented along with another radical (e.g., as in arylalkyl) means a straight or branched, saturated or unsaturated aliphatic divalent radical having the number of atoms indicated or when zero atoms are indicated means a bond (e.g., (C_{6-12})aryl(C_{0-3})alkyl includes phenyl, benzyl, phenethyl, 1-phenylethyl, 3-phenylpropyl, and the like).

"Alkylene", unless indicated otherwise, means a straight or branched, saturated or

unsaturated, aliphatic, divalent radical having the number of carbon atoms indicated (e.g., (C_{2-5})alkylene includes ethylene ($-CH_2CH_2-$ or $-CH(CH_3)-$), 1-methylethylene ($-CH(CH_3)CH_2-$), trimethylene ($-CH_2CH_2CH_2-$), tetramethylene ($-CH_2CH_2CH_2CH_2-$), pentamethylene ($-CH_2CH_2CH_2CH_2CH_2-$), and the like.

"Alkyloxy" means the radical -OR, wherein R is alkyl as defined above, having the number of carbon atoms indicated (e.g., (C_{1-6})alkyloxy includes the radicals methoxy, ethoxy, propoxy, isopropoxy, butoxy, *sec*-butoxy, isobutoxy, *tert*-butoxy, vinyloxy, allyloxy, 1-propenyloxy, isopropenyloxy, 1-butenyloxy, 2-butenyloxy, 3-butenyloxy, 2-methylallyloxy, ethynyloxy, 1-propynyloxy, 2-propynyloxy, and the like).

"Amino" means the radical $-NH_2$. Unless indicated otherwise, the compounds of the invention containing amino moieties include protected derivatives thereof. Suitable protecting groups for amino moieties include acetyl, *tert*-butoxycarbonyl, benzyloxycarbonyl, and the like.

"Animal" includes humans, non-human mammals (e.g., dogs, cats, rabbits, cattle, horses, sheep, goats, swine, deer, and the like) and non-mammals (e.g., birds, and the like).

"Aromatic" means a moiety wherein the constituent atoms make up an unsaturated ring system, all atoms in the ring are sp^2 hybridized and the total number of pi electrons is equal to 4n+2.

"Aryl" means a monocyclic or bicyclic ring assembly (fused or linked by a single bond) containing the total number of ring carbon atoms indicated, wherein each ring is aromatic or when fused with another ring forms an aromatic ring assembly. For example, (C_{6-12})aryl includes phenyl, naphthalenyl, and biphenylyl.

"Bicycloaryl" means a bicyclic ring assembly containing the number of annular carbon atoms indicated, wherein the rings are linked by a single bond or fused and one, but not both, of the rings comprising the assembly is aromatic, and any carbocyclic ketone, thioketone or iminoketone derivative thereof. For example, (C_{9-12})bicycloaryl includes indanyl, indenyl, 1,2,3,4-tetrahydronaphthalenyl, 1,2-dihydronaphthalenyl, cyclohexylphenyl, phenylcyclohexyl, 2,4-dioxo-1,2,3,4-tetrahydro-naphthalenyl, or the like.

"Carbamoyl" means the radical $-C(O)NH_2$. Unless indicated otherwise, the compounds of the invention containing carbamoyl moieties include protected derivatives thereof. Suitable protecting groups for carbamoyl moieties include acetyl, *tert*-butoxycarbonyl, benzyloxycarbonyl, and the like and both the unprotected and protected derivatives fall within the scope of the invention.

"Cycloalkyl" means a saturated or partially unsaturated, monocyclic ring, bicyclic ring assembly (directly linked by a single bond or fused) or bridged polycyclic ring assembly containing the number of annular carbon atoms indicated, and any carbocyclic ketone, thioketone or iminoketone derivative thereof. For example, (C_{3-12})cycloalkyl includes cyclopropyl, cyclobutyl, cyclopentyl, cyclohexyl, cyclohexenyl, 2,5-cyclohexadienyl, bicyclohexylyl, cyclopentylcyclohexyl, bicyclo[2.2.2]octyl, adamantan-1-yl, decahydronaphthalenyl, oxocyclohexyl, dioxocyclohexyl, thiocyclohexyl, 2-oxobicyclo-[2.2.1]hept-1-yl, and the like.

"Cycloalkylene" means a divalent saturated or partially unsaturated, monocyclic ring, bicyclic ring assembly (directly linked by a single bond or fused) or bridged polycyclic ring assembly containing the number of annular carbon atoms indicated, and any carbocyclic ketone, thioketone or iminoketone derivative thereof. For example, (C_{3-12})cycloalkylene includes cyclopropylene, cyclobutylene, cyclopentylene, cyclohexylene, cyclohexenylene, 2,5-cyclohexadienylene, bicyclohexylylene, and the like.

"Disease" specifically includes any unhealthy condition of an animal or part thereof and includes an unhealthy condition that may be caused by, or incident to, medical or veterinary therapy applied to that animal, i.e., the "side effects" of such therapy.

"Halo" means fluoro, chloro, bromo or iodo.

"Haloalkyl" or "halo-substituted alkyl" means an alkyl group as defined above that is substituted with a halo group as defined above e.g., trifluoromethyl, fluoroethyl, fluoropropyl, fluorobutyl, and the like.

"Heteroaryl" means aryl, as defined herein, provided that one or more, preferably one to four, of the ring carbon atoms indicated, are replaced by a heteroatom moiety selected from -N=, $-N^{+}(O^{-})=$, -NR-, -O- or -S-, wherein R is hydrogen, (C_{1-6})alkyl or a protecting group, and each ring contained therein is comprised of 5 to 6 annular members (e.g., hetero(C_{5-14})aryl includes thienyl, furyl, pyrrolyl, pyrimidinyl, isoxazolyl, oxazolyl, indolyl, benzo[*b*]thienyl, isobenzofuranyl, purinyl, isoquinolyl, pterdinyl, perimidinyl, imidazolyl, 1-methylimidazolyl, 1-benzylimidazolyl, pyridyl, pyrazolyl, pyrazinyl, tetrazolyl, quinolyl, [2,4']bipyridinylyl, 2-phenylpyridyl, 4-thiazol-4-ylphenyl, 1*H*-imidazol-1-ylphenyl, and the like). Suitable protecting groups include *tert*-butoxycarbonyl, benzyloxycarbonyl, benzyl, 4-methoxybenzyl, 2-nitrobenzyl, and the like.

"Heterobicycloaryl" means bicycloaryl, as defined herein, except one or more of the annular carbon atoms indicated are replaced by a heteroatom moiety selected from -N-, -NR-,

-O- or -S-, wherein R is hydrogen, (C_{1-6})alkyl or a protecting group, and any carbocyclic ketone, thioketone or iminoketone derivative thereof. For example, hetero(C_{8-12})bicycloaryl includes 3,4-dihydro-2*H*-quinolinyl, 5,6,7,8-tetrahydroquinolinyl, 3,4-dihydro-2*H*-[1,8]naphthyridinyl, morpholinylpyridyl, piperidinylphenyl, 1,2,3,4,5,6-hexahydro-[2,2']bipyridinylyl, 2,4-dioxo-3,4-dihydro-2*H*-quinazolinyl, 3-oxo-2,3-dihydrobenzo-[1,4]oxazinyl, and the like.

"Heterocycloalkyl" means cycloalkyl, as defined herein, provided that one or more, preferably one to three, of the annular carbon atoms indicated is replaced by heteroatom moiety selected from -N-, -NR-, -O- or -S-, wherein R is hydrogen, (C_{1-6})alkyl or a protecting group, and any carbocyclic ketone, thioketone or iminoketone derivative thereof (e.g., the term hetero(C_{3-14})cycloalkyl includes piperidyl, pyrrolidinyl, pyrrolinyl, imidazolidinyl, quinuclidinyl, morpholinyl, [1,4']bipiperidinylyl, 1',2'-dihydro-2*H*-[1,4']bipyridinylyl, 1-morpholin-4-ylpiperidinyl, and the like). Suitable protecting groups include *tert*-butoxycarbonyl, benzyloxycarbonyl, benzyl, 4-methoxybenzyl, 2-nitrobenzyl, and the like. For example, a compound of Formula I wherein R^1 is piperidin-4-ylcarbonyl may exist as either the unprotected or a protected derivative, e.g., wherein R^1 is 1-*tert*-butoxycarbonylpiperidin-4-ylcarbonyl, and both the unprotected and protected derivatives fall within the scope of the invention.

"Hydroxy" means the radical -OH. Unless indicated otherwise, the compounds of the invention containing hydroxy radicals include protected derivatives thereof. Suitable protecting groups for hydroxy moieties include benzyl and the like and both the unprotected and protected derivatives fall within the scope of the invention.

"Iminoketone derivative" means a derivative containing the moiety -C(NR)-, wherein R is hydrogen or (C_{1-6})alkyl.

"Isomers" mean compounds of Formula I having identical molecular formulae but differ in the nature or sequence of bonding of their atoms or in the arrangement of their atoms in space. Isomers that differ in the arrangement of their atoms in space are termed "steroisomers". Stereoisomers that are not mirror images of one another are termed "diastereomers" and stereoisomers that are nonsuperimposable mirror images are termed "enantiomers" or sometimes "optical isomers". A carbon atom bonded to four nonidentical substituents is termed a "chiral center". A compound with one chiral center has two enantiomeric forms of opposite chirality is termed a "racemic mixture". A compound that has more than one chiral center has 2^{n-1} enantiomeric pairs, where n is the number of chiral centers. Compounds with

more than one chiral center may exist as ether an individual diasteromer or as a mixture of diastereomers, termed a "diastereomeric mixture". When one chiral center is present a stereoisomer may be characterized by the absolute configuration of that chiral center. Absolute configuration refers to the arrangement in space of the substituents attached to the chiral center. Enantiomers are characterized by the absolute configuration of their chiral centers and described by the *R*- and *S*-sequencing rules of Cahn, Ingold and Prelog. Conventions for stereochemical nomenclature, methods for the determination of stereochemistry and the separation of stereoisomers are well known in the art (e.g., see "Advanced Organic Chemistry", 4th edition, March, Jerry, John Wiley & Sons, New York, 1992). It is understood that the names and illustration used in this Application to describe compounds of Formula I are meant to encompass all possible stereoisomers and any mixture, racemic or otherwise, thereof.

"Ketone derivative" means a derivative containing the moiety -C(O)-.

"Leaving group" has the meaning conventionally associated with it in synthetic organic chemistry, i.e., an atom or group displaceable under alkylating conditions, and includes, halogen, hydroxy, alkyloxy, alkylsulfonyloxy (e.g., mesyloxy, ethanesulfonyloxy, or the like), arylsulfonyloxy (e.g., benzenesulfonyloxy and tosyloxy, thienyloxy), dihalophosphinoyloxy, tetrahalophosphaoxy, and the like.

"Nitro" means the radical $-NO_2$.

"Optional" or "optionally" means that the subsequently described event or circumstance may or may not occur, and that the description includes instances where the event or circumstance occurs and instances in which it does not. For example, the phrase "any 1 to 3 annular atoms of any aromatic ring with available valences comprising R^6 optionally independently is substituted" means that the aromatic ring referred to may or may not be substituted in order to fall within the scope of the invention.

"*N*-oxide derivatives" means derivatives of compounds of Formula I in which nitrogen atom(s) is in an oxidized state (i.e., $N \rightarrow O$) and which possess the desired pharmacological activity. The n-oxide derivative of a compound of Formula I is within the scope of this invention.

"Oxo" means the radical =O.

"Pathology" of a disease means the essential nature, causes and development of the disease as well as the structural and functional changes that result from the disease processes.

"Pharmaceutically acceptable" means that which is useful in preparing a pharmaceutical composition that is generally safe, non-toxic and neither biologically nor otherwise undesirable

and includes that which is acceptable for veterinary use as well as human pharmaceutical use.

"Pharmaceutically acceptable salts" means salts of compounds of Formula I which are pharmaceutically acceptable, as defined above, and which possess the desired pharmacological activity. Such salts include acid addition salts formed with inorganic acids such as hydrochloric acid, hydrobromic acid, sulfuric acid, nitric acid, phosphoric acid, and the like; or with organic acids such as acetic acid, propionic acid, hexanoic acid, heptanoic acid, cyclopentanepropionic acid, glycolic acid, pyruvic acid, lactic acid, malonic acid, succinic acid, malic acid, maleic acid, fumaric acid, tartatic acid, citric acid, benzoic acid, *o*-(4-hydroxybenzoyl)benzoic acid, cinnamic acid, madelic acid, methanesulfonic acid, ethanesulfonic acid, 1,2-ethanedisulfonic acid, 2-hydroxyethanesulfonic acid, benzenesulfonic acid, *p*-chlorobenzenesulfonic acid, 2-naphthalenesulfonic acid, *p*-toluenesulfonic acid, camphorsulfonic acid, 4-methylbicyclo[2.2.2]oct-2-ene-1-carboxylic acid, glucoheptonic acid, 4,4'-methylenebis(3-hydroxy-2-ene-1-carboxylic acid), 3-phenylpropionic acid, trimethylacetic acid, tertiary butylacetic acid, lauryl sulfuric acid, gluconic acid, glutamic acid, hydroxynaphthoic acid, salicylic acid, stearic acid, muconic acid and the like.

Pharmaceutically acceptable salts also include base addition salts which may be formed when acidic protons present are capable of reacting with inorganic or organic bases. Acceptable inorganic bases include sodium hydroxide, sodium carbonate, potassium hydroxide, aluminum hydroxide and calcium hydroxide. Acceptable organic bases include ethanolamine, diethanolamine, triethanolamine, tromethamine, *N*-methylglucamine and the like.

"Prodrug derivatives" means derivatives of compounds of Formula I which are converted *in vivo* to the corresponding non-derivatized form of a compound of Formula I. All prodrugs of a compound of Formula I are within the scope of this invention.

"Protected derivatives" means derivatives of compounds of Formula I in which a reactive site or sites are blocked with protective groups. Protected derivatives of compounds of Formula I are useful in the preparation of compounds of Formula I or in themselves may be active cysteine protease inhibitors. A comprehensive list of suitable protective groups can be found in T.W. Greene and P.G.M. Wuts, *Protective Groups in Organic Synthesis*, John Wiley & Sons, Inc. (3rd Edition) 1999. All protective derivatives of a compound of Formula I are within the scope of this invention.

"Therapeutically effective amount" means that amount which, when administered to an animal for treating a disease, is sufficient to effect such treatment for the disease.

"Thioketone derivative" means a derivative containing the moiety -C(S)-.

"Treatment" or "treating" means any administration of a compound of the present invention and includes:

preventing the disease from occurring in an animal which may be predisposed to the disease but does not yet experience or display the pathology or symptomatology of the disease,

inhibiting the disease in an animal that is experiencing or displaying the pathology or symptomatology of the diseased (i.e., arresting further development of the pathology and/or symptomatology), or

ameliorating the disease in an animal that is experiencing or displaying the pathology or symptomatology of the diseased (i.e., reversing the pathology and/or symptomatology).

Abbreviations used: acetonitrile (ACN); t-butyloxycarbonyl (BOC); dichloromethane (DCM); 2,3-dichloro-5,6-dicyano-1,4-benzoquinone (DDQ); diisopropylcarbodiimide (DIC); 4-dimethylamino-pyridine (DMAP); electrospray ionization (ESI); diethyl ether (Et_2O); High performance liquid chromatography (HPLC); Liquid Chromatography/Mass Spectroscopy (LC/MS); tetrahydrofuran (THF); trifluoroacetic acid (TFA); tetrapyrrolidinophosphonium hexafluorophosphate (PyBOP); *N*-{(dimethylamino)(1*H*-1,2,3-triazole[4,5-*b*]pyridin-1-yl)-methylene}-*N*-methylmethan-aminium hexafluorophosphate *N*-oxide (HATU); 4-dimethylamino-pyridine (DMAP); dicyclohexylcarbodiimide (DCC); dimethylformamide (DMF).

Nomenclature:

The compounds of Formula I and the intermediates and starting materials used in their preparation are named in accordance with IUPAC rules of nomenclature in which the characteristic groups have decreasing priority for citation as the principle group as follows: acids, esters, amides, etc. Alternatively, the compounds are named by AutoNom 2.1 or 4.0 (Beilstein Information System, Inc.). For example, compounds of Formula I in which:

R^1 is 4-methoxy-benzyl; R^2 is 4-phenylethyl; R^3 is cyclohexylmethyl; and R^4 is acetyl is named 2-acetylamino-3-cyclohexyl-*N*-[2-(4-methoxy-phenylsulfomoyl)-ethyl]-propionamide; or R^1 is 4-methoxy-benzyl; R^2 is 4-phenylethyl; R^3 is isobutyl; and R^4 is pyridine-3-carbonyl is named *N*-(1-{1-[(4-methoxy-phenylsulfamoyl)-methyl]-3-phenyl-propylcarbamoyl}-3-methyl-butyl)-nicotinamide.

Presently Preferred Embodiments:

While the broadest definition of this invention is set forth in the Summary of the Invention, certain aspects of the invention are preferred. Preferred aspects of the invention are the compounds of Formula I in which:

R^1 is $-R^8$, $-X^2OR^8$, $-X^2C(O)R^8$, $-X^2C(OR^7)R^7R^8$, $-X^2NR^7R^8$ or $-X^2NR^7C(O)OR^8$; wherein X^2 is (C_{1-6})alkylene; R^7 is hydrogen or (C_{1-6})alkyl; R^8 is hydrogen, (C_{1-6})alkyl, (C_{3-12})cycloalkyl(C_{0-3})alkyl, hetero(C_{5-12})cycloalkyl(C_{0-3})alkyl, (C_{6-12})aryl(C_{0-3})alkyl or hetero(C_{5-12})aryl(C_{0-3})alkyl; wherein within R^8 said cycloalkyl, heterocycloalkyl, aryl or heteroaryl ring may be substituted with halo, $-R^9$, $-X^3OR^9$, $-X^3C(O)R^9$, $-X^3C(OR^9)R^9$, $-X^3NR^9R^{10}$ or $-X^3NR^9C(O)OR^9$; wherein X^3 is a bond or (C_{1-6})alkylene, R^9 is hydrogen or (C_{1-6})alkyl and R^{10} is cycloalkyl;

R^2 is hydrogen;

R^3 is $-R^{11}$, $-X^3NR^{11}R^{12}$ or $-X^3NR^{12}C(O)OR^{11}$; wherein X^3 is a bond or (C_{1-6})alkylene, R^{11} is hydrogen, (C_{1-6})alkyl, halo(C_{1-6})alkyl, (C_{3-12})cycloalkyl(C_{0-3})alkyl, hetero(C_{5-12})cycloalkyl(C_{0-3})alkyl, (C_{6-12})aryl(C_{0-3})alkyl, hetero(C_{5-12})aryl(C_{0-3})alkyl, (C_{9-12})bicycloaryl(C_{0-3})alkyl or hetero(C_{8-12})bicycloaryl(C_{0-3})alkyl and R^{12} is hydrogen or (C_{1-6})alkyl, wherein any 1 to 3 annular atoms of any aromatic ring with available valences comprising R^3 are optionally independently substituted with halo, nitro, cyano, (C_{1-6})alkyl, halo-substituted(C_{1-6})alkyl, $-OR^7$, $-C(O)R^7$, $-C(O)OR^7$, $-C(O)NR^7R^7$, $-S(O)_2NR^7R^7$, $-X^2NR^7R^7$, $-X^2NR^7C(O)OR^7$, $-X^2NR^7C(O)NR^7R^7$ or $-X^2NR^7C(NR^7NR^7R^7$, wherein X^2 and $R^7$are as defined above;

R^4 is hydrogen or (C_{1-6})alkyl;

R^5 is (C_{1-6})alkyl, halo(C_{1-6})alkyl, (C_{3-12})cycloalkyl(C_{0-3})alkyl, or $-X^2S(O)R^{14}$ where X^2 is as defined above and R^{14} is (C_{3-12})cycloalkyl(C_{0-3})alkyl, hetero(C_{5-12})cycloalkyl(C_{0-3})alkyl, (C_{6-12})aryl(C_{0-3})alkyl, hetero(C_{5-12})aryl(C_{0-3})alkyl, (C_{9-12})bicycloaryl(C_{0-3})alkyl or hetero(C_{8-12})bicycloaryl(C_{0-3})alkyl; preferably, R^5 is (C_{1-6})alkyl or (C_{3-12})cycloalkyl(C_{0-3})alkyl; or

R^4 and R^5 together with the carbon atom to which R^4 and R^5 are attached form (C_{3-7})cycloalkylene;

R^6 is hydrogen or $-X^4X^5R^{13}$, wherein X^4 is -C(O)-, X^5 is a bond, -O- or $-NR^{12}$-, wherein R^{12} is as defined above, and R^{13} is (C_{1-6})alkyl or $-R^{14}$ wherein R^{14} is (C_{3-12})cycloalkyl(C_{0-3})-alkyl, hetero(C_{5-12})cycloalkyl(C_{0-3})alkyl, (C_{6-12})aryl(C_{0-3})alkyl, hetero(C_{5-12})aryl(C_{0-3})alkyl, (C_{9-12})bicycloaryl(C_{0-3})alkyl or hetero(C_{8-12})bicycloaryl(C_{0-3})alkyl; and within R^{14} said

cycloalkyl, heterocycloalkyl, aryl, heteroaryl, bicycloaryl or heterobicycloaryl ring may be substituted with $-OCF_3$, $-CF_3$, -OH, halo, $-R^{16}$, $-X^3OR^{16}$, $-X^3OR^{15}$, $-X^3C(O)R^{15}$, $-R^{15}$, $-X^3C(O)R^{16}$, $-X^3C(O)OR^{15}$, $-X^3NR^{15}R^{15}$, $-X^3NR^{15}C(O)OR^{15}$, wherein X^3 is as defined above, R^{15} is hydrogen or (C_{1-6})alkyl; and R^{16} is (C_{3-12})cycloalkyl(C_{0-3})alkyl, hetero(C_{5-12})cycloalkyl-(C_{0-3})alkyl, (C_{6-12})aryl(C_{0-3})alkyl or hetero(C_{5-12})aryl(C_{0-3})alkyl, and within R^{16} said cycloalkyl, heterocycloalkyl, aryl or heteroaryl ring may be substituted with $-R^{15}$, $-R^{17}$, $-X^3NR^{15}R^{17}$, $-X^3NR^{15}R^{15}$ wherein X^3 and R^{15} are as defined above and R^{17} is (C_{3-12})cycloalkyl(C_{0-3})alkyl, hetero(C_{5-12})cycloalkyl(C_{0-3})alkyl, (C_{6-12})aryl(C_{0-3})alkyl or hetero(C_{5-12})aryl(C_{0-3})alkyl; with the proviso that only one (C_{9-12})bicycloaryl(C_{0-3})alkyl or hetero(C_{8-12})bicycloaryl(C_{0-3})alkyl is present within R^6; and the pharmaceutically acceptable salts thereof.

More preferably, R^1 is 4-methoxyphenyl, 3-methoxyphenyl, 2-methoxyphenyl, 4-chlorophenyl, 3-chloro-phenyl, 2-chlorophenyl, 4-hydroxyphenyl, 2-acetylphenyl, 2-(1-hydroxyethyl)phenyl, 2-phenylaminoethyl, pyridin-4-ylphenyl, pyridin-3-ylphenyl, pyridin-2-ylphenyl, 1H-imidazol-2-yl, piperidin-4-yl or 1-methylpiperidin-4-yl;

R^2 is hydrogen;

R^3 is hydrogen, phenethyl, 4-aminobutyl, butyl or 4-benzyloxycarbonylaminobutyl;

R^4 is hydrogen;

R^5 is isobutyl, *sec*-butyl or cyclohexylmethyl; or R^4 and R^5 together with the carbon atom to which R^4 and R^5 are attached form cyclohexyl; and

R^6 is selected from the group consisting of benzoyl, morpholin-4-ylcarbonyl, acetyl, furan-3-ylcarbonyl, 2-methoxybenzoyl, 3-methoxybenzoyl, naphthalen-2-ylcarbonyl, benzo[1,3]dioxol-5-ylcarbonyl, 3-pyridin-3-ylacryloyl, benzofuran-2-ylcarbonyl, furan-2-ylcarbonyl, *tert*-butoxycarbonyl, biphenyl-4-carbonyl, quinolin-2-ylcarbonyl, quinolin-3-ylcarbonyl, 3-acetylbenzoyl, 4-phenoxybenzoyl, 3-hydroxybenzoyl, 4-hydroxybenzoyl, pyridin-3-ylcarbonyl, 3-(*tert*-butoxycarbonylaminomethyl)benzoyl, 4-carbonylpiperazin-1-ylcarboxylic acid *tert*-butyl ester, 4-carbonylpiperazin-1-ylcarboxylic acid ethyl ester, 4-(furan-2-ylcarbonyl)piperazin-1-ylcarbonyl, pyridin-4-ylcarbonyl, 1-oxypyridin-4-ylcarbonyl, 1-oxypyridin-3-ylcarbonyl, thiophen-2-ylcarbonyl, thiophen-3-ylcarbonyl, 4-benzoylbenzoyl, 5-methylthiophen-2-ylcarbonyl, 3-chlorothiophen-2-ylcarbonyl, 3-bromothiophen-2-ylcarbonyl, 4-chlorobenzoyl, 3-flouro-4-methoxybenzoyl, 4-methoxy-benzoyl, 4-triflouromethoxybenzoyl, 3,4-diflourobenzoyl, 4-fluorobenzoyl, 3,4-dimethoxy-benzoyl, 3-methylbenzoyl, 4-bromobenzoyl, 4-triflouromethylbenzoyl, 3-benzoylbenzoyl, cyclopentanecarbonyl, benzo[b]thiophen-2-ylcarbonyl, 3-chlorobenzo[b]thiophen-2-ylcarbonyl, formamylmethyl

ester, 4-methylpentanoyl, formamylisobutyl ester, formamylmonoallyl ester, formamylisopropyl ester, *N*,*N*-dimethylformamyl, *N*-isopropylformamyl, *N*-pyridin-4-yl-formamyl, *N*-pyridin-3-ylformamyl, 3-phenylacryloyl, 1H-indol-5-ylcarbonyl, pyridin-2-ylcarbonyl, pyrazin-2-ylcarbonyl, 3-hydroxypyridin-2-ylcarbonyl, 2-aminopyridin-3-ylcarbonyl, 2-hydroxypyridin-3-ylcarbonyl, 6-aminopyridin-3-ylcarbonyl, 6-hydroxypyridin-3-ylcarbonyl, pyridazin-4-ylcarbonyl, 3-phenoxybenzoyl, 1-oxo-1,3-dihydroisoindol-2-ylcarbonyl, 4-(4-methylpiperazin-1-yl)benzoyl, 4-morpholin-4-ylbenzoyl, 4-[2-(pyridin-3-ylamino)thiazol-4-yl]-benzoyl, 4-(2-dimethylaminothiazol-4-yl)benzoyl, quinolin-6-ylcarbonyl, 4-dimethylamino-benzoyl, 3-aminobenzoyl, 4-methylpiperazin-1-ylcarbonyl and benzylacetyl.

More preferably, R^1 is 4-methoxyphenyl, 3-methoxyphenyl, 2-methoxyphenyl, 4-chlorophenyl, 3-chloro-phenyl, 2-chlorophenyl, 4-hydroxyphenyl, 2-acetylphenyl, 2-(1-hydroxyethyl)phenyl, 2-phenylaminoethyl, pyridin-4-ylphenyl, pyridin-3-ylphenyl, pyridin-2-ylphenyl, 1H-imidazol-2-yl, piperidin-4-yl or 1-methylpiperidin-4-yl;

R^2 is hydrogen;

R^3 is benzylsulfonylmethyl;

R^4 is hydrogen;

R^5 is isobutyl, *sec*-butyl or cyclohexylmethyl; or R^4 and R^5 together with the carbon atom to which R^4 and R^5 are attached form cyclohexyl; and

R^6 is selected from the group consisting of R^6 is selected from the group consisting of benzoyl, morpholin-4-ylcarbonyl, acetyl, furan-3-ylcarbonyl, 2-methoxybenzoyl, 3-methoxybenzoyl, naphthalen-2-ylcarbonyl, benzo[1,3]dioxol-5-ylcarbonyl, 3-pyridin-3-ylacryloyl, benzofuran-2-ylcarbonyl, furan-2-ylcarbonyl, *tert*-butoxycarbonyl, biphenyl-4-carbonyl, quinolin-2-ylcarbonyl, quinolin-3-ylcarbonyl, 3-acetylbenzoyl, 4-phenoxybenzoyl, 3-hydroxybenzoyl, 4-hydroxybenzoyl, pyridin-3-ylcarbonyl, 3-(*tert*-butoxycarbonylaminomethyl)benzoyl, 4-carbonylpiperazin-1-ylcarboxylic acid *tert*-butyl ester, 4-carbonylpiperazin-1-ylcarboxylic acid ethyl ester, 4-(furan-2-ylcarbonyl)piperazin-1-ylcarbonyl, pyridin-4-ylcarbonyl, 1-oxypyridin-4-ylcarbonyl, 1-oxypyridin-3-ylcarbonyl, thiophen-2-ylcarbonyl, thiophen-3-ylcarbonyl, 4-benzoylbenzoyl, 5-methylthiophen-2-ylcarbonyl, 3-chlorothiophen-2-ylcarbonyl, 3-bromothiophen-2-ylcarbonyl, 4-chlorobenzoyl, 3-flouro-4-methoxybenzoyl, 4-methoxy-benzoyl, 4-triflouromethoxybenzoyl, 3,4-diflourobenzoyl, 4-fluorobenzoyl, 3,4-dimethoxy-benzoyl, 3-methylbenzoyl, 4-bromobenzoyl, 4-triflouromethylbenzoyl, 3-benzoylbenzoyl, cyclopentanecarbonyl, benzo[b]thiophen-2-ylcarbonyl, 3-chlorobenzo[b]thiophen-2-ylcarbonyl, formamylmethyl ester, 4-methylpentanoyl,

formamylisobutyl ester, formamylmonoallyl ester, formamylisopropyl ester, *N,N*-dimethylformamyl, *N*-isopropylformamyl, *N*-pyridin-4-yl-formamyl, *N*-pyridin-3-ylformamyl, 3-phenylacryloyl, 1H-indol-5-ylcarbonyl, pyridin-2-ylcarbonyl, pyrazin-2-ylcarbonyl, 3-hydroxypyridin-2-ylcarbonyl, 2-aminopyridin-3-ylcarbonyl, 2-hydroxypyridin-3-ylcarbonyl, 6-aminopyridin-3-ylcarbonyl, 6-hydroxypyridin-3-ylcarbonyl, pyridazin-4-ylcarbonyl, 3-phenoxybenzoyl, 1-oxo-1,3-dihydroisoindol-2-ylcarbonyl, 4-(4-methylpiperazin-1-yl)benzoyl, 4-morpholin-4-ylbenzoyl, 4-[2-(pyridin-3-ylamino)thiazol-4-yl]-benzoyl, 4-(2-dimethylaminothiazol-4-yl)benzoyl, quinolin-6-ylcarbonyl, 4-dimethylamino-benzoyl, 3-aminobenzoyl, 4-methylpiperazin-1-ylcarbonyl and benzylacetyl.

Even more preferably, R^1 is 4-methoxyphenyl, 3-acetylphenyl, 3-(1-hydroxyethyl)-phenyl, 2-(phenylamino)ethyl or 4-hydroxyphenyl;

R^2 is hydrogen;

R^3 is hydrogen, 2-phenethyl, 4-aminobutyl, or 4-benzyloxycarbonylaminobutyl;

R^4 is hydrogen;

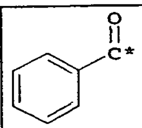
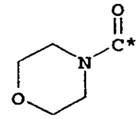
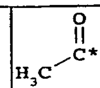
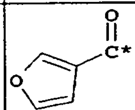
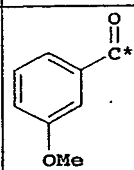
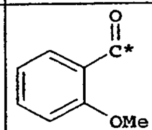
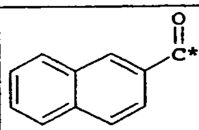
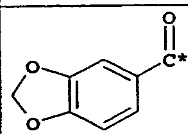
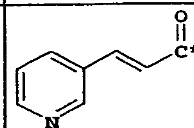
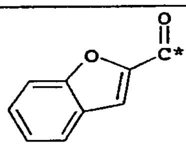
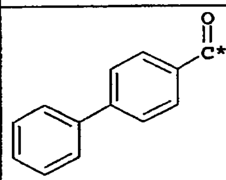
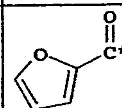
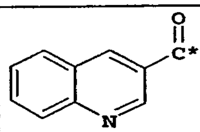
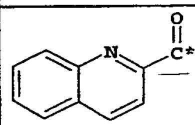
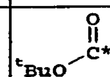
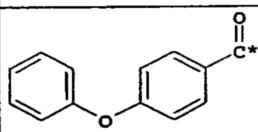
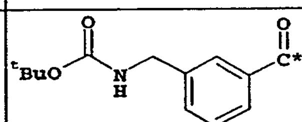
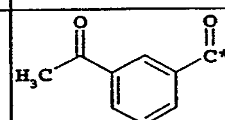
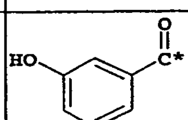
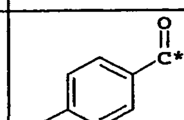
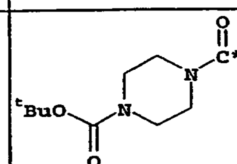
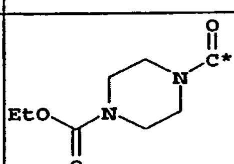
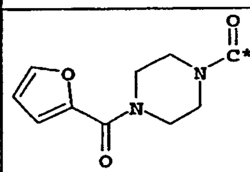
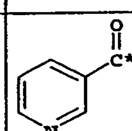
R^5 is isobutyl, *sec*-butyl or cyclohexylmethyl; or R^4 and R^5 together with the carbon atom to which R^4 and R^5 are attached form cyclohexyl; and

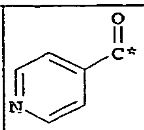
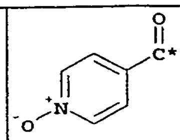
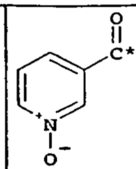
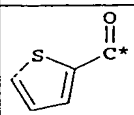
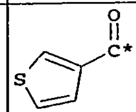
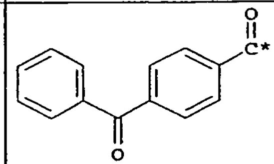
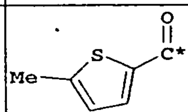
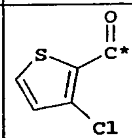
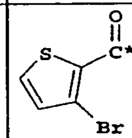
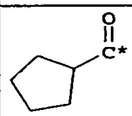
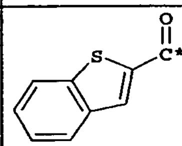
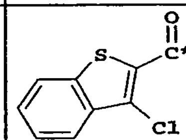
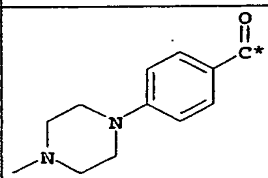
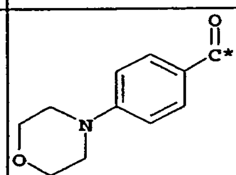
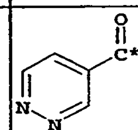
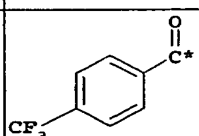
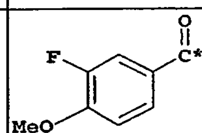
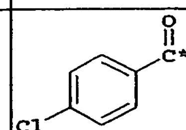
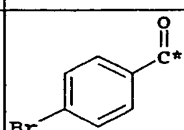
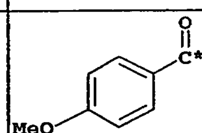
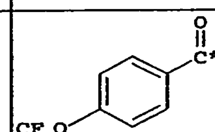
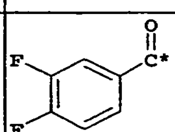
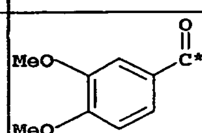
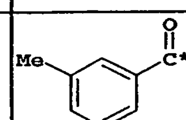
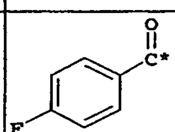
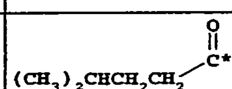
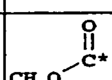
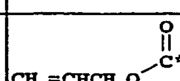
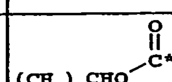
R^6 is selected from the group consisting of acetyl, pyridin-3-ylcarbonyl, 3-(*tert*-butoxycarbonylamino)benzoyl, pyridin-4-ylcarbonyl, 1H-indol-5-ylcarbonyl, benzyloxycarbonyl, 3-aminobenzoyl, 4-methylpiperazin-1-ylcarbonyl, quinolin-6-ylcarbonyl, 4-[2-(pyridin-3-ylamino)thiazol-4-yl]benzoyl, 4-dimethylaminobenzoyl, morpholin-4-yl-carbonyl, 4-(2-dimethylaminothiazol-4-yl)benzoyl, *tert*-butoxycarbonyl, 4-(4-ethylpiperazin-1-yl)-benzoyl, and 4-[2-(4-methylpiperazin-1-yl)thiazol-4-yl]benzoyl.

A number of different preferences have been given above, and following any one of these preferences results in a compound of this invention that is more presently preferred than a compound in which that particular preference is not followed. However, these preferences are generally independent [although some (alternative) preferences are mutually exclusive], and additive; and following more than one of these preferences may result in a more presently preferred compound than one in which fewer of the preferences are followed.

Particular compounds of the invention are selected from the compounds formed by joining C* of one of the fragments (A1 to A77) shown in Table 1 to the nitrogen atom (*N) of one of the fragments (B1 to B4) shown in Table 2, and joining the methine carbon atom (CH*) of one of the fragments (B1 to B4) shown in Table 2 to the acyl carbon atom (C*) of one of the fragments (C1 to C31) depicted in Table 3.

TABLE 1

A1		A2		A3	
A4		A5		A6	
A7		A8		A9	
A10		A11		A12	
A13		A14		A15	
A16		A17		A18	
A19		A20		A21	
A22		A23		A24	

A25		A26		A27	
A28		A29		A30	
A31		A32		A33	
A34		A35		A36	
A37		A38		A39	
A40		A41		A42	
A43		A44		A45	
A46		A47		A48	
A49		A50		A51	
A52		A53		A54	

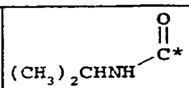
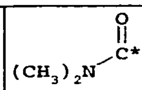
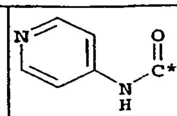
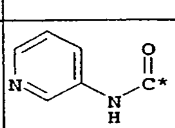
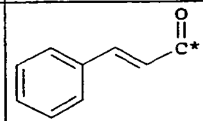
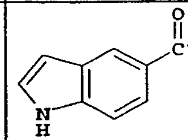
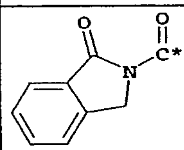
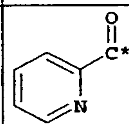
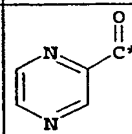
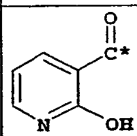
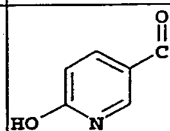
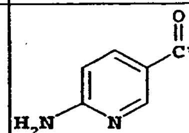
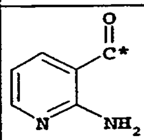
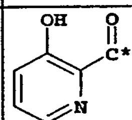
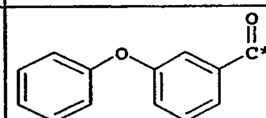
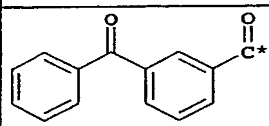
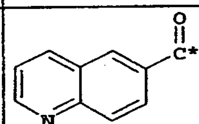
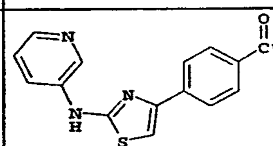
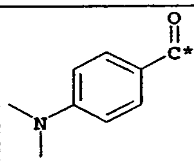
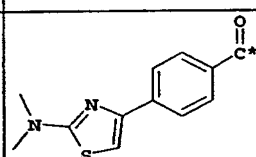
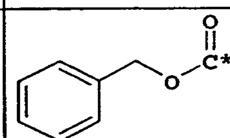
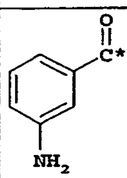
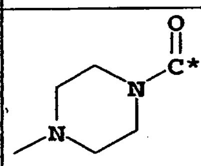
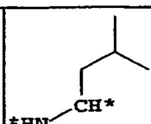
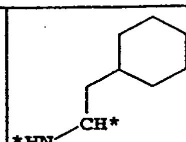
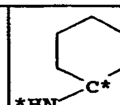
A55		A56		A57	
A58		A59		A60	
A61		A62		A63	
A64		A65		A66	
A67		A68		A69	
A70		A71		A72	
A73		A74		A75	
A76		A77			

TABLE 2

B1		B2		B3	

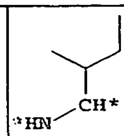
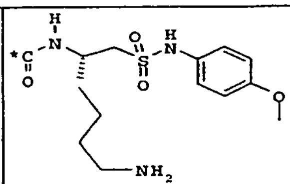
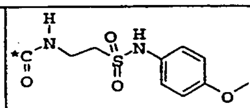
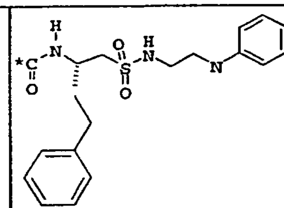
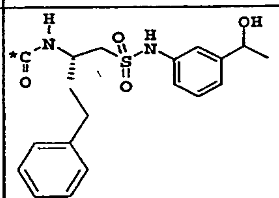
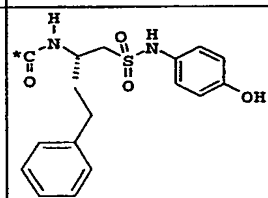
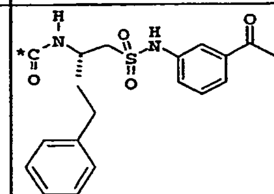
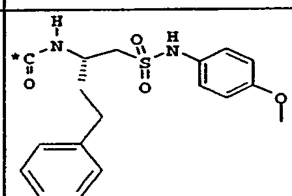
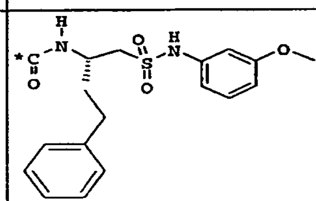
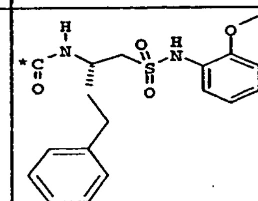
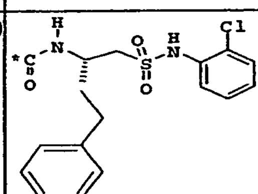
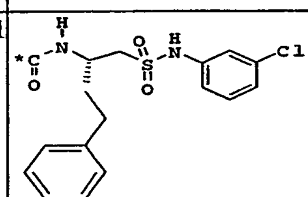
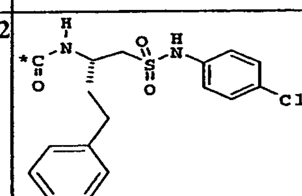
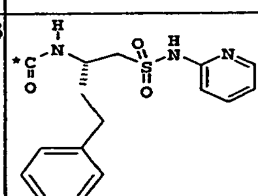
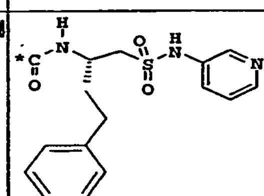
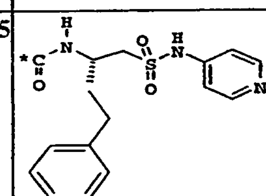
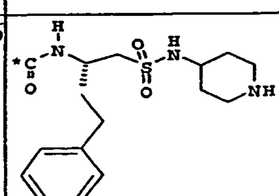
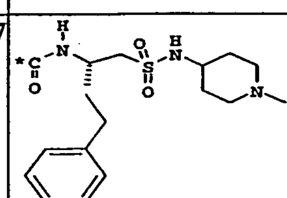
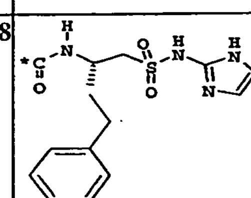
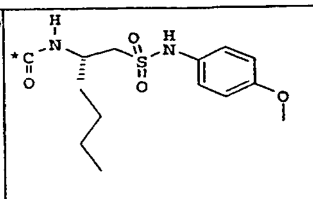
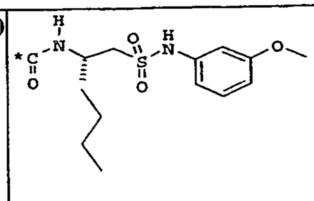
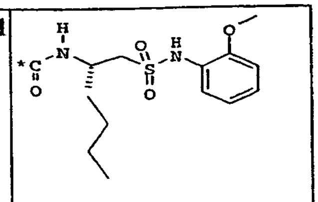
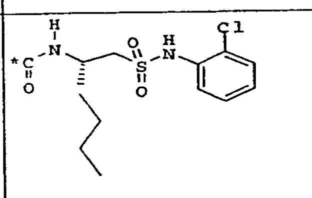
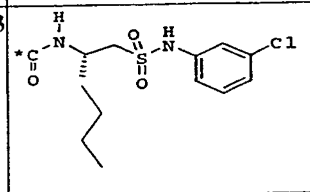
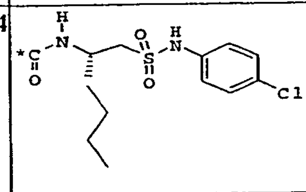
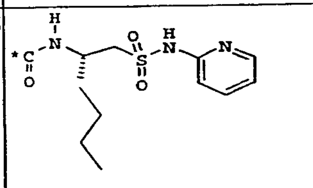
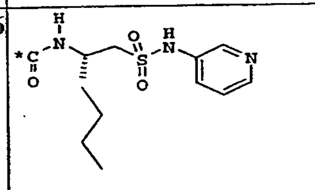
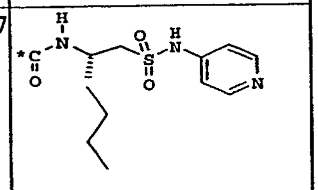
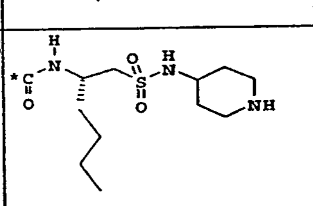
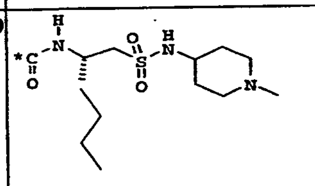
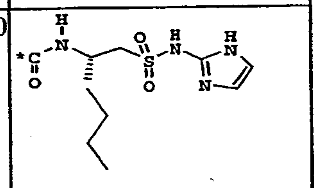
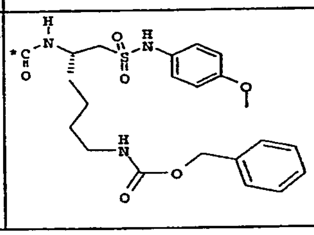
B4					

TABLE 3

C1		C2		C3	
C4		C5		C6	
C7		C8		C9	
C10		C11		C12	
C13		C14		C15	
C16		C17		C18	

C19		C20		C21	
C22		C23		C24	
C25		C26		C27	
C28		C29		C30	
C31					

Particularly preferred compounds of "A", "B", and "C" combinations are illustrated in table 4, infra:

Table 4

A1-B1-C1
A2-B1-C1
A3-B1-C1
A4-B1-C1
A5-B1-C1
A6-B1-C1
A7-B1-C1
A8-B1-C1
A9-B1-C1
A10-B1-C1
A11-B1-C1
A12-B1-C1
A13-B1-C1
A14-B1-C1
A15-B1-C1
A16-B1-C1
A17-B1-C1
A18-B1-C1
A19-B1-C1
A20-B1-C1
A21-B1-C1
A22-B1-C1
A23-B1-C1
A24-B1-C1
A25-B1-C1
A26-B1-C1
A27-B1-C1
A28-B1-C1
A29-B1-C1
A30-B1-C1
A31-B1-C1
A32-B1-C1
A33-B1-C1
A34-B1-C1
A35-B1-C1
A36-B1-C1
A37-B1-C1
A38-B1-C1
A39-B1-C1
A40-B1-C1
A41-B1-C1
A42-B1-C1
A43-B1-C1
A44-B1-C1
A45-B1-C1
A46-B1-C1
A47-B1-C1
A48-B1-C1
A49-B1-C1
A50-B1-C1
A51-B1-C1
A52-B1-C1
A53-B1-C1
A54-B1-C1
A55-B1-C1
A56-B1-C1
A57-B1-C1
A58-B1-C1
A59-B1-C1
A60-B1-C1
A61-B1-C1
A62-B1-C1
A63-B1-C1
A64-B1-C1
A65-B1-C1
A66-B1-C1
A67-B1-C1
A68-B1-C1

A69-B1-C1
A70-B1-C1
A71-B1-C1
A72-B1-C1
A73-B1-C1
A74-B1-C1
A75-B1-C1
A76-B1-C1
A77-B1-C1
A1-B2-C1
A2-B2-C1
A3-B2-C1
A4-B2-C1
A5-B2-C1
A6-B2-C1
A7-B2-C1
A8-B2-C1
A9-B2-C1
A10-B2-C1
A11-B2-C1
A12-B2-C1
A13-B2-C1
A14-B2-C1
A15-B2-C1
A16-B2-C1
A17-B2-C1
A18-B2-C1
A19-B2-C1
A20-B2-C1
A21-B2-C1
A22-B2-C1
A23-B2-C1
A24-B2-C1
A25-B2-C1
A26-B2-C1
A27-B2-C1
A28-B2-C1
A29-B2-C1
A30-B2-C1
A31-B2-C1
A32-B2-C1
A33-B2-C1
A34-B2-C1
A35-B2-C1
A36-B2-C1
A37-B2-C1
A38-B2-C1
A39-B2-C1
A40-B2-C1
A41-B2-C1
A42-B2-C1
A43-B2-C1
A44-B2-C1
A45-B2-C1
A46-B2-C1
A47-B2-C1
A48-B2-C1
A49-B2-C1
A50-B2-C1
A51-B2-C1
A52-B2-C1
A53-B2-C1
A54-B2-C1
A55-B2-C1
A56-B2-C1
A57-B2-C1
A58-B2-C1
A59-B2-C1
A60-B2-C1
A61-B2-C1
A62-B2-C1
A63-B2-C1
A64-B2-C1
A65-B2-C1
A66-B2-C1
A67-B2-C1
A68-B2-C1
A69-B2-C1
A70-B2-C1
A71-B2-C1
A72-B2-C1
A73-B2-C1
A74-B2-C1
A75-B2-C1
A76-B2-C1
A77-B2-C1
A1-B3-C1
A2-B3-C1
A3-B3-C1
A4-B3-C1
A5-B3-C1
A6-B3-C1
A7-B3-C1
A8-B3-C1
A9-B3-C1
A10-B3-C1
A11-B3-C1
A12-B3-C1
A13-B3-C1
A14-B3-C1
A15-B3-C1
A16-B3-C1
A17-B3-C1
A18-B3-C1
A19-B3-C1
A20-B3-C1
A21-B3-C1
A22-B3-C1
A23-B3-C1
A24-B3-C1
A25-B3-C1
A26-B3-C1
A27-B3-C1
A28-B3-C1
A29-B3-C1
A30-B3-C1
A31-B3-C1
A32-B3-C1
A33-B3-C1
A34-B3-C1
A35-B3-C1
A36-B3-C1
A37-B3-C1
A38-B3-C1
A39-B3-C1
A40-B3-C1
A41-B3-C1
A42-B3-C1
A43-B3-C1
A44-B3-C1
A45-B3-C1
A46-B3-C1
A47-B3-C1
A48-B3-C1
A49-B3-C1
A50-B3-C1
A51-B3-C1
A52-B3-C1
A53-B3-C1
A54-B3-C1
A55-B3-C1
A56-B3-C1
A57-B3-C1
A58-B3-C1
A59-B3-C1
A60-B3-C1
A61-B3-C1
A62-B3-C1
A63-B3-C1
A64-B3-C1
A65-B3-C1
A66-B3-C1
A67-B3-C1
A68-B3-C1
A69-B3-C1
A70-B3-C1
A71-B3-C1
A72-B3-C1
A73-B3-C1
A74-B3-C1
A75-B3-C1
A76-B3-C1
A77-B3-C1
A1-B4-C1
A2-B4-C1
A3-B4-C1
A4-B4-C1
A5-B4-C1
A6-B4-C1
A7-B4-C1
A8-B4-C1
A9-B4-C1
A10-B4-C1
A11-B4-C1
A12-B4-C1
A13-B4-C1
A14-B4-C1
A15-B4-C1
A16-B4-C1
A17-B4-C1
A18-B4-C1
A19-B4-C1
A20-B4-C1
A21-B4-C1
A22-B4-C1
A23-B4-C1
A24-B4-C1
A25-B4-C1
A26-B4-C1
A27-B4-C1
A28-B4-C1
A29-B4-C1
A30-B4-C1
A31-B4-C1
A32-B4-C1
A33-B4-C1
A34-B4-C1
A35-B4-C1
A36-B4-C1
A37-B4-C1
A38-B4-C1
A39-B4-C1
A40-B4-C1
A41-B4-C1
A42-B4-C1
A43-B4-C1
A44-B4-C1
A45-B4-C1
A46-B4-C1
A47-B4-C1
A48-B4-C1
A49-B4-C1
A50-B4-C1
A51-B4-C1
A52-B4-C1
A53-B4-C1
A54-B4-C1
A55-B4-C1
A56-B4-C1
A57-B4-C1
A58-B4-C1
A59-B4-C1
A60-B4-C1
A61-B4-C1
A62-B4-C1
A63-B4-C1
A64-B4-C1
A65-B4-C1
A66-B4-C1
A67-B4-C1
A68-B4-C1
A69-B4-C1
A70-B4-C1
A71-B4-C1
A72-B4-C1
A73-B4-C1
A74-B4-C1
A75-B4-C1
A76-B4-C1
A77-B4-C1
A1-B1-C2
A2-B1-C2
A3-B1-C2
A4-B1-C2
A5-B1-C2
A6-B1-C2
A7-B1-C2
A8-B1-C2
A9-B1-C2
A10-B1-C2
A11-B1-C2
A12-B1-C2
A13-B1-C2
A14-B1-C2
A15-B1-C2
A16-B1-C2
A17-B1-C2
A18-B1-C2
A19-B1-C2
A20-B1-C2
A21-B1-C2
A22-B1-C2
A23-B1-C2
A24-B1-C2

A25-B1-C2
A26-B1-C2
A27-B1-C2
A28-B1-C2
A29-B1-C2
A30-B1-C2
A31-B1-C2
A32-B1-C2
A33-B1-C2
A34-B1-C2
A35-B1-C2
A36-B1-C2
A37-B1-C2
A38-B1-C2
A39-B1-C2
A40-B1-C2
A41-B1-C2
A42-B1-C2
A43-B1-C2
A44-B1-C2
A45-B1-C2
A46-B1-C2
A47-B1-C2
A48-B1-C2
A49-B1-C2
A50-B1-C2
A51-B1-C2
A52-B1-C2
A53-B1-C2
A54-B1-C2
A55-B1-C2
A56-B1-C2
A57-B1-C2
A58-B1-C2
A59-B1-C2
A60-B1-C2
A61-B1-C2
A62-B1-C2
A63-B1-C2
A64-B1-C2
A65-B1-C2
A66-B1-C2
A67-B1-C2
A68-B1-C2
A69-B1-C2
A70-B1-C2
A71-B1-C2
A72-B1-C2
A73-B1-C2
A74-B1-C2
A75-B1-C2
A76-B1-C2
A77-B1-C2
A1-B2-C2
A2-B2-C2
A3-B2-C2
A4-B2-C2
A5-B2-C2
A6-B2-C2
A7-B2-C2
A8-B2-C2
A9-B2-C2
A10-B2-C2
A11-B2-C2
A12-B2-C2
A13-B2-C2
A14-B2-C2
A15-B2-C2
A16-B2-C2
A17-B2-C2
A18-B2-C2
A19-B2-C2
A20-B2-C2
A21-B2-C2
A22-B2-C2
A23-B2-C2
A24-B2-C2
A25-B2-C2
A26-B2-C2
A27-B2-C2
A28-B2-C2
A29-B2-C2
A30-B2-C2
A31-B2-C2
A32-B2-C2
A33-B2-C2
A34-B2-C2
A35-B2-C2
A36-B2-C2
A37-B2-C2
A38-B2-C2
A39-B2-C2
A40-B2-C2
A41-B2-C2
A42-B2-C2
A43-B2-C2
A44-B2-C2
A45-B2-C2
A46-B2-C2
A47-B2-C2
A48-B2-C2
A49-B2-C2
A50-B2-C2
A51-B2-C2
A52-B2-C2
A53-B2-C2
A54-B2-C2
A55-B2-C2
A56-B2-C2
A57-B2-C2
A58-B2-C2
A59-B2-C2
A60-B2-C2
A61-B2-C2
A62-B2-C2
A63-B2-C2
A64-B2-C2
A65-B2-C2
A66-B2-C2
A67-B2-C2
A68-B2-C2
A69-B2-C2
A70-B2-C2
A71-B2-C2
A72-B2-C2
A73-B2-C2
A74-B2-C2
A75-B2-C2
A76-B2-C2
A77-B2-C2
A1-B3-C2
A2-B3-C2
A3-B3-C2
A4-B3-C2
A5-B3-C2
A6-B3-C2
A7-B3-C2
A8-B3-C2
A9-B3-C2
A10-B3-C2
A11-B3-C2
A12-B3-C2
A13-B3-C2
A14-B3-C2
A15-B3-C2
A16-B3-C2
A17-B3-C2
A18-B3-C2
A19-B3-C2
A20-B3-C2
A21-B3-C2
A22-B3-C2
A23-B3-C2
A24-B3-C2
A25-B3-C2
A26-B3-C2
A27-B3-C2
A28-B3-C2
A29-B3-C2
A30-B3-C2
A31-B3-C2
A32-B3-C2
A33-B3-C2
A34-B3-C2
A35-B3-C2
A36-B3-C2
A37-B3-C2
A38-B3-C2
A39-B3-C2
A40-B3-C2
A41-B3-C2
A42-B3-C2
A43-B3-C2
A44-B3-C2
A45-B3-C2
A46-B3-C2
A47-B3-C2
A48-B3-C2
A49-B3-C2
A50-B3-C2
A51-B3-C2
A52-B3-C2
A53-B3-C2
A54-B3-C2
A55-B3-C2
A56-B3-C2
A57-B3-C2
A58-B3-C2
A59-B3-C2
A60-B3-C2
A61-B3-C2
A62-B3-C2
A63-B3-C2
A64-B3-C2
A65-B3-C2
A66-B3-C2
A67-B3-C2
A68-B3-C2
A69-B3-C2
A70-B3-C2
A71-B3-C2
A72-B3-C2
A73-B3-C2
A74-B3-C2
A75-B3-C2
A76-B3-C2
A77-B3-C2
A1-B4-C2
A2-B4-C2
A3-B4-C2
A4-B4-C2
A5-B4-C2
A6-B4-C2
A7-B4-C2
A8-B4-C2
A9-B4-C2
A10-B4-C2
A11-B4-C2
A12-B4-C2
A13-B4-C2
A14-B4-C2
A15-B4-C2
A16-B4-C2
A17-B4-C2
A18-B4-C2
A19-B4-C2
A20-B4-C2
A21-B4-C2
A22-B4-C2
A23-B4-C2
A24-B4-C2
A25-B4-C2
A26-B4-C2
A27-B4-C2
A28-B4-C2
A29-B4-C2
A30-B4-C2
A31-B4-C2
A32-B4-C2
A33-B4-C2
A34-B4-C2
A35-B4-C2
A36-B4-C2
A37-B4-C2
A38-B4-C2
A39-B4-C2
A40-B4-C2
A41-B4-C2
A42-B4-C2
A43-B4-C2
A44-B4-C2
A45-B4-C2
A46-B4-C2
A47-B4-C2
A48-B4-C2
A49-B4-C2
A50-B4-C2
A51-B4-C2
A52-B4-C2
A53-B4-C2
A54-B4-C2
A55-B4-C2
A56-B4-C2
A57-B4-C2

A58-B4-C2
A59-B4-C2
A60-B4-C2
A61-B4-C2
A62-B4-C2
A63-B4-C2
A64-B4-C2
A65-B4-C2
A66-B4-C2
A67-B4-C2
A68-B4-C2
A69-B4-C2
A70-B4-C2
A71-B4-C2
A72-B4-C2
A73-B4-C2
A74-B4-C2
A75-B4-C2
A76-B4-C2
A77-B4-C2
A1-B1-C3
A2-B1-C3
A3-B1-C3
A4-B1-C3
A5-B1-C3
A6-B1-C3
A7-B1-C3
A8-B1-C3
A9-B1-C3
A10-B1-C3
A11-B1-C3
A12-B1-C3
A13-B1-C3
A14-B1-C3
A15-B1-C3
A16-B1-C3
A17-B1-C3
A18-B1-C3
A19-B1-C3
A20-B1-C3
A21-B1-C3
A22-B1-C3
A23-B1-C3
A24-B1-C3
A25-B1-C3
A26-B1-C3
A27-B1-C3
A28-B1-C3
A29-B1-C3
A30-B1-C3
A31-B1-C3
A32-B1-C3
A33-B1-C3
A34-B1-C3
A35-B1-C3
A36-B1-C3
A37-B1-C3
A38-B1-C3
A39-B1-C3
A40-B1-C3
A41-B1-C3
A42-B1-C3
A43-B1-C3
A44-B1-C3
A45-B1-C3
A46-B1-C3
A47-B1-C3
A48-B1-C3
A49-B1-C3
A50-B1-C3
A51-B1-C3
A52-B1-C3
A53-B1-C3
A54-B1-C3
A55-B1-C3
A56-B1-C3
A57-B1-C3
A58-B1-C3
A59-B1-C3
A60-B1-C3
A61-B1-C3
A62-B1-C3
A63-B1-C3
A64-B1-C3
A65-B1-C3
A66-B1-C3
A67-B1-C3
A68-B1-C3
A69-B1-C3
A70-B1-C3
A71-B1-C3
A72-B1-C3
A73-B1-C3
A74-B1-C3
A75-B1-C3
A76-B1-C3
A77-B1-C3
A1-B2-C3
A2-B2-C3
A3-B2-C3
A4-B2-C3
A5-B2-C3
A6-B2-C3
A7-B2-C3
A8-B2-C3
A9-B2-C3
A10-B2-C3
A11-B2-C3
A12-B2-C3
A13-B2-C3
A14-B2-C3
A15-B2-C3
A16-B2-C3
A17-B2-C3
A18-B2-C3
A19-B2-C3
A20-B2-C3
A21-B2-C3
A22-B2-C3
A23-B2-C3
A24-B2-C3
A25-B2-C3
A26-B2-C3
A27-B2-C3
A28-B2-C3
A29-B2-C3
A30-B2-C3
A31-B2-C3
A32-B2-C3
A33-B2-C3
A34-B2-C3
A35-B2-C3
A36-B2-C3
A37-B2-C3
A38-B2-C3
A39-B2-C3
A40-B2-C3
A41-B2-C3
A42-B2-C3
A43-B2-C3
A44-B2-C3
A45-B2-C3
A46-B2-C3
A47-B2-C3
A48-B2-C3
A49-B2-C3
A50-B2-C3
A51-B2-C3
A52-B2-C3
A53-B2-C3
A54-B2-C3
A55-B2-C3
A56-B2-C3
A57-B2-C3
A58-B2-C3
A59-B2-C3
A60-B2-C3
A61-B2-C3
A62-B2-C3
A63-B2-C3
A64-B2-C3
A65-B2-C3
A66-B2-C3
A67-B2-C3
A68-B2-C3
A69-B2-C3
A70-B2-C3
A71-B2-C3
A72-B2-C3
A73-B2-C3
A74-B2-C3
A75-B2-C3
A76-B2-C3
A77-B2-C3
A1-B3-C3
A2-B3-C3
A3-B3-C3
A4-B3-C3
A5-B3-C3
A6-B3-C3
A7-B3-C3
A8-B3-C3
A9-B3-C3
A10-B3-C3
A11-B3-C3
A12-B3-C3
A13-B3-C3
A14-B3-C3
A15-B3-C3
A16-B3-C3
A17-B3-C3
A18-B3-C3
A19-B3-C3
A20-B3-C3
A21-B3-C3
A22-B3-C3
A23-B3-C3
A24-B3-C3
A25-B3-C3
A26-B3-C3
A27-B3-C3
A28-B3-C3
A29-B3-C3
A30-B3-C3
A31-B3-C3
A32-B3-C3
A33-B3-C3
A34-B3-C3
A35-B3-C3
A36-B3-C3
A37-B3-C3
A38-B3-C3
A39-B3-C3
A40-B3-C3
A41-B3-C3
A42-B3-C3
A43-B3-C3
A44-B3-C3
A45-B3-C3
A46-B3-C3
A47-B3-C3
A48-B3-C3
A49-B3-C3
A50-B3-C3
A51-B3-C3
A52-B3-C3
A53-B3-C3
A54-B3-C3
A55-B3-C3
A56-B3-C3
A57-B3-C3
A58-B3-C3
A59-B3-C3
A60-B3-C3
A61-B3-C3
A62-B3-C3
A63-B3-C3
A64-B3-C3
A65-B3-C3
A66-B3-C3
A67-B3-C3
A68-B3-C3
A69-B3-C3
A70-B3-C3
A71-B3-C3
A72-B3-C3
A73-B3-C3
A74-B3-C3
A75-B3-C3
A76-B3-C3
A77-B3-C3
A1-B4-C3
A2-B4-C3
A3-B4-C3
A4-B4-C3
A5-B4-C3
A6-B4-C3
A7-B4-C3
A8-B4-C3
A9-B4-C3
A10-B4-C3
A11-B4-C3
A12-B4-C3
A13-B4-C3

A14-B4-C3
A15-B4-C3
A16-B4-C3
A17-B4-C3
A18-B4-C3
A19-B4-C3
A20-B4-C3
A21-B4-C3
A22-B4-C3
A23-B4-C3
A24-B4-C3
A25-B4-C3
A26-B4-C3
A27-B4-C3
A28-B4-C3
A29-B4-C3
A30-B4-C3
A31-B4-C3
A32-B4-C3
A33-B4-C3
A34-B4-C3
A35-B4-C3
A36-B4-C3
A37-B4-C3
A38-B4-C3
A39-B4-C3
A40-B4-C3
A41-B4-C3
A42-B4-C3
A43-B4-C3
A44-B4-C3
A45-B4-C3
A46-B4-C3
A47-B4-C3
A48-B4-C3
A49-B4-C3
A50-B4-C3
A51-B4-C3
A52-B4-C3
A53-B4-C3
A54-B4-C3
A55-B4-C3
A56-B4-C3
A57-B4-C3
A58-B4-C3
A59-B4-C3
A60-B4-C3
A61-B4-C3
A62-B4-C3
A63-B4-C3
A64-B4-C3
A65-B4-C3
A66-B4-C3
A67-B4-C3
A68-B4-C3
A69-B4-C3
A70-B4-C3
A71-B4-C3
A72-B4-C3
A73-B4-C3
A74-B4-C3
A75-B4-C3
A76-B4-C3
A77-B4-C3
A1-B1-C4
A2-B1-C4
A3-B1-C4
A4-B1-C4
A5-B1-C4
A6-B1-C4
A7-B1-C4
A8-B1-C4
A9-B1-C4
A10-B1-C4
A11-B1-C4
A12-B1-C4
A13-B1-C4
A14-B1-C4
A15-B1-C4
A16-B1-C4
A17-B1-C4
A18-B1-C4
A19-B1-C4
A20-B1-C4
A21-B1-C4
A22-B1-C4
A23-B1-C4
A24-B1-C4
A25-B1-C4
A26-B1-C4
A27-B1-C4
A28-B1-C4
A29-B1-C4
A30-B1-C4
A31-B1-C4
A32-B1-C4
A33-B1-C4
A34-B1-C4
A35-B1-C4
A36-B1-C4
A37-B1-C4
A38-B1-C4
A39-B1-C4
A40-B1-C4
A41-B1-C4
A42-B1-C4
A43-B1-C4
A44-B1-C4
A45-B1-C4
A46-B1-C4
A47-B1-C4
A48-B1-C4
A49-B1-C4
A50-B1-C4
A51-B1-C4
A52-B1-C4
A53-B1-C4
A54-B1-C4
A55-B1-C4
A56-B1-C4
A57-B1-C4
A58-B1-C4
A59-B1-C4
A60-B1-C4
A61-B1-C4
A62-B1-C4
A63-B1-C4
A64-B1-C4
A65-B1-C4
A66-B1-C4
A67-B1-C4
A68-B1-C4
A69-B1-C4
A70-B1-C4
A71-B1-C4
A72-B1-C4
A73-B1-C4
A74-B1-C4
A75-B1-C4
A76-B1-C4
A77-B1-C4
A1-B2-C4
A2-B2-C4
A3-B2-C4
A4-B2-C4
A5-B2-C4
A6-B2-C4
A7-B2-C4
A8-B2-C4
A9-B2-C4
A10-B2-C4
A11-B2-C4
A12-B2-C4
A13-B2-C4
A14-B2-C4
A15-B2-C4
A16-B2-C4
A17-B2-C4
A18-B2-C4
A19-B2-C4
A20-B2-C4
A21-B2-C4
A22-B2-C4
A23-B2-C4
A24-B2-C4
A25-B2-C4
A26-B2-C4
A27-B2-C4
A28-B2-C4
A29-B2-C4
A30-B2-C4
A31-B2-C4
A32-B2-C4
A33-B2-C4
A34-B2-C4
A35-B2-C4
A36-B2-C4
A37-B2-C4
A38-B2-C4
A39-B2-C4
A40-B2-C4
A41-B2-C4
A42-B2-C4
A43-B2-C4
A44-B2-C4
A45-B2-C4
A46-B2-C4
A47-B2-C4
A48-B2-C4
A49-B2-C4
A50-B2-C4
A51-B2-C4
A52-B2-C4
A53-B2-C4
A54-B2-C4
A55-B2-C4
A56-B2-C4
A57-B2-C4
A58-B2-C4
A59-B2-C4
A60-B2-C4
A61-B2-C4
A62-B2-C4
A63-B2-C4
A64-B2-C4
A65-B2-C4
A66-B2-C4
A67-B2-C4
A68-B2-C4
A69-B2-C4
A70-B2-C4
A71-B2-C4
A72-B2-C4
A73-B2-C4
A74-B2-C4
A75-B2-C4
A76-B2-C4
A77-B2-C4
A1-B3-C4
A2-B3-C4
A3-B3-C4
A4-B3-C4
A5-B3-C4
A6-B3-C4
A7-B3-C4
A8-B3-C4
A9-B3-C4
A10-B3-C4
A11-B3-C4
A12-B3-C4
A13-B3-C4
A14-B3-C4
A15-B3-C4
A16-B3-C4
A17-B3-C4
A18-B3-C4
A19-B3-C4
A20-B3-C4
A21-B3-C4
A22-B3-C4
A23-B3-C4
A24-B3-C4
A25-B3-C4
A26-B3-C4
A27-B3-C4
A28-B3-C4
A29-B3-C4
A30-B3-C4
A31-B3-C4
A32-B3-C4
A33-B3-C4
A34-B3-C4
A35-B3-C4
A36-B3-C4
A37-B3-C4
A38-B3-C4
A39-B3-C4
A40-B3-C4
A41-B3-C4
A42-B3-C4
A43-B3-C4
A44-B3-C4
A45-B3-C4
A46-B3-C4

A47-B3-C4
A48-B3-C4
A49-B3-C4
A50-B3-C4
A51-B3-C4
A52-B3-C4
A53-B3-C4
A54-B3-C4
A55-B3-C4
A56-B3-C4
A57-B3-C4
A58-B3-C4
A59-B3-C4
A60-B3-C4
A61-B3-C4
A62-B3-C4
A63-B3-C4
A64-B3-C4
A65-B3-C4
A66-B3-C4
A67-B3-C4
A68-B3-C4
A69-B3-C4
A70-B3-C4
A71-B3-C4
A72-B3-C4
A73-B3-C4
A74-B3-C4
A75-B3-C4
A76-B3-C4
A77-B3-C4
A1-B4-C4
A2-B4-C4
A3-B4-C4
A4-B4-C4
A5-B4-C4
A6-B4-C4
A7-B4-C4
A8-B4-C4
A9-B4-C4
A10-B4-C4
A11-B4-C4
A12-B4-C4
A13-B4-C4
A14-B4-C4
A15-B4-C4
A16-B4-C4
A17-B4-C4
A18-B4-C4
A19-B4-C4
A20-B4-C4
A21-B4-C4
A22-B4-C4
A23-B4-C4
A24-B4-C4
A25-B4-C4
A26-B4-C4
A27-B4-C4
A28-B4-C4
A29-B4-C4
A30-B4-C4
A31-B4-C4
A32-B4-C4
A33-B4-C4
A34-B4-C4
A35-B4-C4
A36-B4-C4
A37-B4-C4
A38-B4-C4
A39-B4-C4
A40-B4-C4
A41-B4-C4
A42-B4-C4
A43-B4-C4
A44-B4-C4
A45-B4-C4
A46-B4-C4
A47-B4-C4
A48-B4-C4
A49-B4-C4
A50-B4-C4
A51-B4-C4
A52-B4-C4
A53-B4-C4
A54-B4-C4
A55-B4-C4
A56-B4-C4
A57-B4-C4
A58-B4-C4
A59-B4-C4
A60-B4-C4
A61-B4-C4
A62-B4-C4
A63-B4-C4
A64-B4-C4
A65-B4-C4
A66-B4-C4
A67-B4-C4
A68-B4-C4
A69-B4-C4
A70-B4-C4
A71-B4-C4
A72-B4-C4
A73-B4-C4
A74-B4-C4
A75-B4-C4
A76-B4-C4
A77-B4-C4
A1-B1-C5
A2-B1-C5
A3-B1-C5
A4-B1-C5
A5-B1-C5
A6-B1-C5
A7-B1-C5
A8-B1-C5
A9-B1-C5
A10-B1-C5
A11-B1-C5
A12-B1-C5
A13-B1-C5
A14-B1-C5
A15-B1-C5
A16-B1-C5
A17-B1-C5
A18-B1-C5
A19-B1-C5
A20-B1-C5
A21-B1-C5
A22-B1-C5
A23-B1-C5
A24-B1-C5
A25-B1-C5
A26-B1-C5
A27-B1-C5
A28-B1-C5
A29-B1-C5
A30-B1-C5
A31-B1-C5
A32-B1-C5
A33-B1-C5
A34-B1-C5
A35-B1-C5
A36-B1-C5
A37-B1-C5
A38-B1-C5
A39-B1-C5
A40-B1-C5
A41-B1-C5
A42-B1-C5
A43-B1-C5
A44-B1-C5
A45-B1-C5
A46-B1-C5
A47-B1-C5
A48-B1-C5
A49-B1-C5
A50-B1-C5
A51-B1-C5
A52-B1-C5
A53-B1-C5
A54-B1-C5
A55-B1-C5
A56-B1-C5
A57-B1-C5
A58-B1-C5
A59-B1-C5
A60-B1-C5
A61-B1-C5
A62-B1-C5
A63-B1-C5
A64-B1-C5
A65-B1-C5
A66-B1-C5
A67-B1-C5
A68-B1-C5
A69-B1-C5
A70-B1-C5
A71-B1-C5
A72-B1-C5
A73-B1-C5
A74-B1-C5
A75-B1-C5
A76-B1-C5
A77-B1-C5
A1-B2-C5
A2-B2-C5
A3-B2-C5
A4-B2-C5
A5-B2-C5
A6-B2-C5
A7-B2-C5
A8-B2-C5
A9-B2-C5
A10-B2-C5
A11-B2-C5
A12-B2-C5
A13-B2-C5
A14-B2-C5
A15-B2-C5
A16-B2-C5
A17-B2-C5
A18-B2-C5
A19-B2-C5
A20-B2-C5
A21-B2-C5
A22-B2-C5
A23-B2-C5
A24-B2-C5
A25-B2-C5
A26-B2-C5
A27-B2-C5
A28-B2-C5
A29-B2-C5
A30-B2-C5
A31-B2-C5
A32-B2-C5
A33-B2-C5
A34-B2-C5
A35-B2-C5
A36-B2-C5
A37-B2-C5
A38-B2-C5
A39-B2-C5
A40-B2-C5
A41-B2-C5
A42-B2-C5
A43-B2-C5
A44-B2-C5
A45-B2-C5
A46-B2-C5
A47-B2-C5
A48-B2-C5
A49-B2-C5
A50-B2-C5
A51-B2-C5
A52-B2-C5
A53-B2-C5
A54-B2-C5
A55-B2-C5
A56-B2-C5
A57-B2-C5
A58-B2-C5
A59-B2-C5
A60-B2-C5
A61-B2-C5
A62-B2-C5
A63-B2-C5
A64-B2-C5
A65-B2-C5
A66-B2-C5
A67-B2-C5
A68-B2-C5
A69-B2-C5
A70-B2-C5
A71-B2-C5
A72-B2-C5
A73-B2-C5
A74-B2-C5
A75-B2-C5
A76-B2-C5
A77-B2-C5
A1-B3-C5
A2-B3-C5

A3-B3-C5
A4-B3-C5
A5-B3-C5
A6-B3-C5
A7-B3-C5
A8-B3-C5
A9-B3-C5
A10-B3-C5
A11-B3-C5
A12-B3-C5
A13-B3-C5
A14-B3-C5
A15-B3-C5
A16-B3-C5
A17-B3-C5
A18-B3-C5
A19-B3-C5
A20-B3-C5
A21-B3-C5
A22-B3-C5
A23-B3-C5
A24-B3-C5
A25-B3-C5
A26-B3-C5
A27-B3-C5
A28-B3-C5
A29-B3-C5
A30-B3-C5
A31-B3-C5
A32-B3-C5
A33-B3-C5
A34-B3-C5
A35-B3-C5
A36-B3-C5
A37-B3-C5
A38-B3-C5
A39-B3-C5
A40-B3-C5
A41-B3-C5
A42-B3-C5
A43-B3-C5
A44-B3-C5
A45-B3-C5
A46-B3-C5
A47-B3-C5
A48-B3-C5
A49-B3-C5
A50-B3-C5
A51-B3-C5
A52-B3-C5
A53-B3-C5
A54-B3-C5
A55-B3-C5
A56-B3-C5
A57-B3-C5
A58-B3-C5
A59-B3-C5
A60-B3-C5
A61-B3-C5
A62-B3-C5
A63-B3-C5
A64-B3-C5
A65-B3-C5
A66-B3-C5
A67-B3-C5
A68-B3-C5
A69-B3-C5
A70-B3-C5
A71-B3-C5
A72-B3-C5
A73-B3-C5
A74-B3-C5
A75-B3-C5
A76-B3-C5
A77-B3-C5
A1-B4-C5
A2-B4-C5
A3-B4-C5
A4-B4-C5
A5-B4-C5
A6-B4-C5
A7-B4-C5
A8-B4-C5
A9-B4-C5
A10-B4-C5
A11-B4-C5
A12-B4-C5
A13-B4-C5
A14-B4-C5
A15-B4-C5
A16-B4-C5
A17-B4-C5
A18-B4-C5
A19-B4-C5
A20-B4-C5
A21-B4-C5
A22-B4-C5
A23-B4-C5
A24-B4-C5
A25-B4-C5
A26-B4-C5
A27-B4-C5
A28-B4-C5
A29-B4-C5
A30-B4-C5
A31-B4-C5
A32-B4-C5
A33-B4-C5
A34-B4-C5
A35-B4-C5
A36-B4-C5
A37-B4-C5
A38-B4-C5
A39-B4-C5
A40-B4-C5
A41-B4-C5
A42-B4-C5
A43-B4-C5
A44-B4-C5
A45-B4-C5
A46-B4-C5
A47-B4-C5
A48-B4-C5
A49-B4-C5
A50-B4-C5
A51-B4-C5
A52-B4-C5
A53-B4-C5
A54-B4-C5
A55-B4-C5
A56-B4-C5
A57-B4-C5
A58-B4-C5
A59-B4-C5
A60-B4-C5
A61-B4-C5
A62-B4-C5
A63-B4-C5
A64-B4-C5
A65-B4-C5
A66-B4-C5
A67-B4-C5
A68-B4-C5
A69-B4-C5
A70-B4-C5
A71-B4-C5
A72-B4-C5
A73-B4-C5
A74-B4-C5
A75-B4-C5
A76-B4-C5
A77-B4-C5
A1-B1-C6
A2-B1-C6
A3-B1-C6
A4-B1-C6
A5-B1-C6
A6-B1-C6
A7-B1-C6
A8-B1-C6
A9-B1-C6
A10-B1-C6
A11-B1-C6
A12-B1-C6
A13-B1-C6
A14-B1-C6
A15-B1-C6
A16-B1-C6
A17-B1-C6
A18-B1-C6
A19-B1-C6
A20-B1-C6
A21-B1-C6
A22-B1-C6
A23-B1-C6
A24-B1-C6
A25-B1-C6
A26-B1-C6
A27-B1-C6
A28-B1-C6
A29-B1-C6
A30-B1-C6
A31-B1-C6
A32-B1-C6
A33-B1-C6
A34-B1-C6
A35-B1-C6
A36-B1-C6
A37-B1-C6
A38-B1-C6
A39-B1-C6
A40-B1-C6
A41-B1-C6
A42-B1-C6
A43-B1-C6
A44-B1-C6
A45-B1-C6
A46-B1-C6
A47-B1-C6
A48-B1-C6
A49-B1-C6
A50-B1-C6
A51-B1-C6
A52-B1-C6
A53-B1-C6
A54-B1-C6
A55-B1-C6
A56-B1-C6
A57-B1-C6
A58-B1-C6
A59-B1-C6
A60-B1-C6
A61-B1-C6
A62-B1-C6
A63-B1-C6
A64-B1-C6
A65-B1-C6
A66-B1-C6
A67-B1-C6
A68-B1-C6
A69-B1-C6
A70-B1-C6
A71-B1-C6
A72-B1-C6
A73-B1-C6
A74-B1-C6
A75-B1-C6
A76-B1-C6
A77-B1-C6
A1-B2-C6
A2-B2-C6
A3-B2-C6
A4-B2-C6
A5-B2-C6
A6-B2-C6
A7-B2-C6
A8-B2-C6
A9-B2-C6
A10-B2-C6
A11-B2-C6
A12-B2-C6
A13-B2-C6
A14-B2-C6
A15-B2-C6
A16-B2-C6
A17-B2-C6
A18-B2-C6
A19-B2-C6
A20-B2-C6
A21-B2-C6
A22-B2-C6
A23-B2-C6
A24-B2-C6
A25-B2-C6
A26-B2-C6
A27-B2-C6
A28-B2-C6
A29-B2-C6
A30-B2-C6
A31-B2-C6
A32-B2-C6
A33-B2-C6
A34-B2-C6
A35-B2-C6

A36-B2-C6
A37-B2-C6
A38-B2-C6
A39-B2-C6
A40-B2-C6
A41-B2-C6
A42-B2-C6
A43-B2-C6
A44-B2-C6
A45-B2-C6
A46-B2-C6
A47-B2-C6
A48-B2-C6
A49-B2-C6
A50-B2-C6
A51-B2-C6
A52-B2-C6
A53-B2-C6
A54-B2-C6
A55-B2-C6
A56-B2-C6
A57-B2-C6
A58-B2-C6
A59-B2-C6
A60-B2-C6
A61-B2-C6
A62-B2-C6
A63-B2-C6
A64-B2-C6
A65-B2-C6
A66-B2-C6
A67-B2-C6
A68-B2-C6
A69-B2-C6
A70-B2-C6
A71-B2-C6
A72-B2-C6
A73-B2-C6
A74-B2-C6
A75-B2-C6
A76-B2-C6
A77-B2-C6
A1-B3-C6
A2-B3-C6
A3-B3-C6
A4-B3-C6
A5-B3-C6
A6-B3-C6
A7-B3-C6
A8-B3-C6
A9-B3-C6
A10-B3-C6
A11-B3-C6
A12-B3-C6
A13-B3-C6
A14-B3-C6
A15-B3-C6
A16-B3-C6
A17-B3-C6
A18-B3-C6
A19-B3-C6
A20-B3-C6
A21-B3-C6
A22-B3-C6
A23-B3-C6
A24-B3-C6
A25-B3-C6
A26-B3-C6
A27-B3-C6
A28-B3-C6
A29-B3-C6
A30-B3-C6
A31-B3-C6
A32-B3-C6
A33-B3-C6
A34-B3-C6
A35-B3-C6
A36-B3-C6
A37-B3-C6
A38-B3-C6
A39-B3-C6
A40-B3-C6
A41-B3-C6
A42-B3-C6
A43-B3-C6
A44-B3-C6
A45-B3-C6
A46-B3-C6
A47-B3-C6
A48-B3-C6
A49-B3-C6
A50-B3-C6
A51-B3-C6
A52-B3-C6
A53-B3-C6
A54-B3-C6
A55-B3-C6
A56-B3-C6
A57-B3-C6
A58-B3-C6
A59-B3-C6
A60-B3-C6
A61-B3-C6
A62-B3-C6
A63-B3-C6
A64-B3-C6
A65-B3-C6
A66-B3-C6
A67-B3-C6
A68-B3-C6
A69-B3-C6
A70-B3-C6
A71-B3-C6
A72-B3-C6
A73-B3-C6
A74-B3-C6
A75-B3-C6
A76-B3-C6
A77-B3-C6
A1-B4-C6
A2-B4-C6
A3-B4-C6
A4-B4-C6
A5-B4-C6
A6-B4-C6
A7-B4-C6
A8-B4-C6
A9-B4-C6
A10-B4-C6
A11-B4-C6
A12-B4-C6
A13-B4-C6
A14-B4-C6
A15-B4-C6
A16-B4-C6
A17-B4-C6
A18-B4-C6
A19-B4-C6
A20-B4-C6
A21-B4-C6
A22-B4-C6
A23-B4-C6
A24-B4-C6
A25-B4-C6
A26-B4-C6
A27-B4-C6
A28-B4-C6
A29-B4-C6
A30-B4-C6
A31-B4-C6
A32-B4-C6
A33-B4-C6
A34-B4-C6
A35-B4-C6
A36-B4-C6
A37-B4-C6
A38-B4-C6
A39-B4-C6
A40-B4-C6
A41-B4-C6
A42-B4-C6
A43-B4-C6
A44-B4-C6
A45-B4-C6
A46-B4-C6
A47-B4-C6
A48-B4-C6
A49-B4-C6
A50-B4-C6
A51-B4-C6
A52-B4-C6
A53-B4-C6
A54-B4-C6
A55-B4-C6
A56-B4-C6
A57-B4-C6
A58-B4-C6
A59-B4-C6
A60-B4-C6
A61-B4-C6
A62-B4-C6
A63-B4-C6
A64-B4-C6
A65-B4-C6
A66-B4-C6
A67-B4-C6
A68-B4-C6
A69-B4-C6
A70-B4-C6
A71-B4-C6
A72-B4-C6
A73-B4-C6
A74-B4-C6
A75-B4-C6
A76-B4-C6
A77-B4-C6
A1-B1-C7
A2-B1-C7
A3-B1-C7
A4-B1-C7
A5-B1-C7
A6-B1-C7
A7-B1-C7
A8-B1-C7
A9-B1-C7
A10-B1-C7
A11-B1-C7
A12-B1-C7
A13-B1-C7
A14-B1-C7
A15-B1-C7
A16-B1-C7
A17-B1-C7
A18-B1-C7
A19-B1-C7
A20-B1-C7
A21-B1-C7
A22-B1-C7
A23-B1-C7
A24-B1-C7
A25-B1-C7
A26-B1-C7
A27-B1-C7
A28-B1-C7
A29-B1-C7
A30-B1-C7
A31-B1-C7
A32-B1-C7
A33-B1-C7
A34-B1-C7
A35-B1-C7
A36-B1-C7
A37-B1-C7
A38-B1-C7
A39-B1-C7
A40-B1-C7
A41-B1-C7
A42-B1-C7
A43-B1-C7
A44-B1-C7
A45-B1-C7
A46-B1-C7
A47-B1-C7
A48-B1-C7
A49-B1-C7
A50-B1-C7
A51-B1-C7
A52-B1-C7
A53-B1-C7
A54-B1-C7
A55-B1-C7
A56-B1-C7
A57-B1-C7
A58-B1-C7
A59-B1-C7
A60-B1-C7
A61-B1-C7
A62-B1-C7
A63-B1-C7
A64-B1-C7
A65-B1-C7
A66-B1-C7
A67-B1-C7
A68-B1-C7

A69-B1-C7
A70-B1-C7
A71-B1-C7
A72-B1-C7
A73-B1-C7
A74-B1-C7
A75-B1-C7
A76-B1-C7
A77-B1-C7
A1-B2-C7
A2-B2-C7
A3-B2-C7
A4-B2-C7
A5-B2-C7
A6-B2-C7
A7-B2-C7
A8-B2-C7
A9-B2-C7
A10-B2-C7
A11-B2-C7
A12-B2-C7
A13-B2-C7
A14-B2-C7
A15-B2-C7
A16-B2-C7
A17-B2-C7
A18-B2-C7
A19-B2-C7
A20-B2-C7
A21-B2-C7
A22-B2-C7
A23-B2-C7
A24-B2-C7
A25-B2-C7
A26-B2-C7
A27-B2-C7
A28-B2-C7
A29-B2-C7
A30-B2-C7
A31-B2-C7
A32-B2-C7
A33-B2-C7
A34-B2-C7
A35-B2-C7
A36-B2-C7
A37-B2-C7
A38-B2-C7
A39-B2-C7
A40-B2-C7
A41-B2-C7
A42-B2-C7
A43-B2-C7
A44-B2-C7
A45-B2-C7
A46-B2-C7
A47-B2-C7
A48-B2-C7
A49-B2-C7
A50-B2-C7
A51-B2-C7
A52-B2-C7
A53-B2-C7
A54-B2-C7
A55-B2-C7
A56-B2-C7
A57-B2-C7
A58-B2-C7
A59-B2-C7
A60-B2-C7
A61-B2-C7
A62-B2-C7
A63-B2-C7
A64-B2-C7
A65-B2-C7
A66-B2-C7
A67-B2-C7
A68-B2-C7
A69-B2-C7
A70-B2-C7
A71-B2-C7
A72-B2-C7
A73-B2-C7
A74-B2-C7
A75-B2-C7
A76-B2-C7
A77-B2-C7
A1-B3-C7
A2-B3-C7
A3-B3-C7
A4-B3-C7
A5-B3-C7
A6-B3-C7
A7-B3-C7
A8-B3-C7
A9-B3-C7
A10-B3-C7
A11-B3-C7
A12-B3-C7
A13-B3-C7
A14-B3-C7
A15-B3-C7
A16-B3-C7
A17-B3-C7
A18-B3-C7
A19-B3-C7
A20-B3-C7
A21-B3-C7
A22-B3-C7
A23-B3-C7
A24-B3-C7
A25-B3-C7
A26-B3-C7
A27-B3-C7
A28-B3-C7
A29-B3-C7
A30-B3-C7
A31-B3-C7
A32-B3-C7
A33-B3-C7
A34-B3-C7
A35-B3-C7
A36-B3-C7
A37-B3-C7
A38-B3-C7
A39-B3-C7
A40-B3-C7
A41-B3-C7
A42-B3-C7
A43-B3-C7
A44-B3-C7
A45-B3-C7
A46-B3-C7
A47-B3-C7
A48-B3-C7
A49-B3-C7
A50-B3-C7
A51-B3-C7
A52-B3-C7
A53-B3-C7
A54-B3-C7
A55-B3-C7
A56-B3-C7
A57-B3-C7
A58-B3-C7
A59-B3-C7
A60-B3-C7
A61-B3-C7
A62-B3-C7
A63-B3-C7
A64-B3-C7
A65-B3-C7
A66-B3-C7
A67-B3-C7
A68-B3-C7
A69-B3-C7
A70-B3-C7
A71-B3-C7
A72-B3-C7
A73-B3-C7
A74-B3-C7
A75-B3-C7
A76-B3-C7
A77-B3-C7
A1-B4-C7
A2-B4-C7
A3-B4-C7
A4-B4-C7
A5-B4-C7
A6-B4-C7
A7-B4-C7
A8-B4-C7
A9-B4-C7
A10-B4-C7
A11-B4-C7
A12-B4-C7
A13-B4-C7
A14-B4-C7
A15-B4-C7
A16-B4-C7
A17-B4-C7
A18-B4-C7
A19-B4-C7
A20-B4-C7
A21-B4-C7
A22-B4-C7
A23-B4-C7
A24-B4-C7
A25-B4-C7
A26-B4-C7
A27-B4-C7
A28-B4-C7
A29-B4-C7
A30-B4-C7
A31-B4-C7
A32-B4-C7
A33-B4-C7
A34-B4-C7
A35-B4-C7
A36-B4-C7
A37-B4-C7
A38-B4-C7
A39-B4-C7
A40-B4-C7
A41-B4-C7
A42-B4-C7
A43-B4-C7
A44-B4-C7
A45-B4-C7
A46-B4-C7
A47-B4-C7
A48-B4-C7
A49-B4-C7
A50-B4-C7
A51-B4-C7
A52-B4-C7
A53-B4-C7
A54-B4-C7
A55-B4-C7
A56-B4-C7
A57-B4-C7
A58-B4-C7
A59-B4-C7
A60-B4-C7
A61-B4-C7
A62-B4-C7
A63-B4-C7
A64-B4-C7
A65-B4-C7
A66-B4-C7
A67-B4-C7
A68-B4-C7
A69-B4-C7
A70-B4-C7
A71-B4-C7
A72-B4-C7
A73-B4-C7
A74-B4-C7
A75-B4-C7
A76-B4-C7
A77-B4-C7
A1-B1-C8
A2-B1-C8
A3-B1-C8
A4-B1-C8
A5-B1-C8
A6-B1-C8
A7-B1-C8
A8-B1-C8
A9-B1-C8
A10-B1-C8
A11-B1-C8
A12-B1-C8
A13-B1-C8
A14-B1-C8
A15-B1-C8
A16-B1-C8
A17-B1-C8
A18-B1-C8
A19-B1-C8
A20-B1-C8
A21-B1-C8
A22-B1-C8
A23-B1-C8
A24-B1-C8

A25-B1-C8
A26-B1-C8
A27-B1-C8
A28-B1-C8
A29-B1-C8
A30-B1-C8
A31-B1-C8
A32-B1-C8
A33-B1-C8
A34-B1-C8
A35-B1-C8
A36-B1-C8
A37-B1-C8
A38-B1-C8
A39-B1-C8
A40-B1-C8
A41-B1-C8
A42-B1-C8
A43-B1-C8
A44-B1-C8
A45-B1-C8
A46-B1-C8
A47-B1-C8
A48-B1-C8
A49-B1-C8
A50-B1-C8
A51-B1-C8
A52-B1-C8
A53-B1-C8
A54-B1-C8
A55-B1-C8
A56-B1-C8
A57-B1-C8
A58-B1-C8
A59-B1-C8
A60-B1-C8
A61-B1-C8
A62-B1-C8
A63-B1-C8
A64-B1-C8
A65-B1-C8
A66-B1-C8
A67-B1-C8
A68-B1-C8
A69-B1-C8
A70-B1-C8
A71-B1-C8
A72-B1-C8
A73-B1-C8
A74-B1-C8
A75-B1-C8
A76-B1-C8
A77-B1-C8
A1-B2-C8
A2-B2-C8
A3-B2-C8
A4-B2-C8
A5-B2-C8
A6-B2-C8
A7-B2-C8
A8-B2-C8
A9-B2-C8
A10-B2-C8
A11-B2-C8
A12-B2-C8
A13-B2-C8
A14-B2-C8
A15-B2-C8
A16-B2-C8
A17-B2-C8
A18-B2-C8
A19-B2-C8
A20-B2-C8
A21-B2-C8
A22-B2-C8
A23-B2-C8
A24-B2-C8
A25-B2-C8
A26-B2-C8
A27-B2-C8
A28-B2-C8
A29-B2-C8
A30-B2-C8
A31-B2-C8
A32-B2-C8
A33-B2-C8
A34-B2-C8
A35-B2-C8
A36-B2-C8
A37-B2-C8
A38-B2-C8
A39-B2-C8
A40-B2-C8
A41-B2-C8
A42-B2-C8
A43-B2-C8
A44-B2-C8
A45-B2-C8
A46-B2-C8
A47-B2-C8
A48-B2-C8
A49-B2-C8
A50-B2-C8
A51-B2-C8
A52-B2-C8
A53-B2-C8
A54-B2-C8
A55-B2-C8
A56-B2-C8
A57-B2-C8
A58-B2-C8
A59-B2-C8
A60-B2-C8
A61-B2-C8
A62-B2-C8
A63-B2-C8
A64-B2-C8
A65-B2-C8
A66-B2-C8
A67-B2-C8
A68-B2-C8
A69-B2-C8
A70-B2-C8
A71-B2-C8
A72-B2-C8
A73-B2-C8
A74-B2-C8
A75-B2-C8
A76-B2-C8
A77-B2-C8
A1-B3-C8
A2-B3-C8
A3-B3-C8
A4-B3-C8
A5-B3-C8
A6-B3-C8
A7-B3-C8
A8-B3-C8
A9-B3-C8
A10-B3-C8
A11-B3-C8
A12-B3-C8
A13-B3-C8
A14-B3-C8
A15-B3-C8
A16-B3-C8
A17-B3-C8
A18-B3-C8
A19-B3-C8
A20-B3-C8
A21-B3-C8
A22-B3-C8
A23-B3-C8
A24-B3-C8
A25-B3-C8
A26-B3-C8
A27-B3-C8
A28-B3-C8
A29-B3-C8
A30-B3-C8
A31-B3-C8
A32-B3-C8
A33-B3-C8
A34-B3-C8
A35-B3-C8
A36-B3-C8
A37-B3-C8
A38-B3-C8
A39-B3-C8
A40-B3-C8
A41-B3-C8
A42-B3-C8
A43-B3-C8
A44-B3-C8
A45-B3-C8
A46-B3-C8
A47-B3-C8
A48-B3-C8
A49-B3-C8
A50-B3-C8
A51-B3-C8
A52-B3-C8
A53-B3-C8
A54-B3-C8
A55-B3-C8
A56-B3-C8
A57-B3-C8
A58-B3-C8
A59-B3-C8
A60-B3-C8
A61-B3-C8
A62-B3-C8
A63-B3-C8
A64-B3-C8
A65-B3-C8
A66-B3-C8
A67-B3-C8
A68-B3-C8
A69-B3-C8
A70-B3-C8
A71-B3-C8
A72-B3-C8
A73-B3-C8
A74-B3-C8
A75-B3-C8
A76-B3-C8
A77-B3-C8
A1-B4-C8
A2-B4-C8
A3-B4-C8
A4-B4-C8
A5-B4-C8
A6-B4-C8
A7-B4-C8
A8-B4-C8
A9-B4-C8
A10-B4-C8
A11-B4-C8
A12-B4-C8
A13-B4-C8
A14-B4-C8
A15-B4-C8
A16-B4-C8
A17-B4-C8
A18-B4-C8
A19-B4-C8
A20-B4-C8
A21-B4-C8
A22-B4-C8
A23-B4-C8
A24-B4-C8
A25-B4-C8
A26-B4-C8
A27-B4-C8
A28-B4-C8
A29-B4-C8
A30-B4-C8
A31-B4-C8
A32-B4-C8
A33-B4-C8
A34-B4-C8
A35-B4-C8
A36-B4-C8
A37-B4-C8
A38-B4-C8
A39-B4-C8
A40-B4-C8
A41-B4-C8
A42-B4-C8
A43-B4-C8
A44-B4-C8
A45-B4-C8
A46-B4-C8
A47-B4-C8
A48-B4-C8
A49-B4-C8
A50-B4-C8
A51-B4-C8
A52-B4-C8
A53-B4-C8
A54-B4-C8
A55-B4-C8
A56-B4-C8
A57-B4-C8

A58-B4-C8
A59-B4-C8
A60-B4-C8
A61-B4-C8
A62-B4-C8
A63-B4-C8
A64-B4-C8
A65-B4-C8
A66-B4-C8
A67-B4-C8
A68-B4-C8
A69-B4-C8
A70-B4-C8
A71-B4-C8
A72-B4-C8
A73-B4-C8
A74-B4-C8
A75-B4-C8
A76-B4-C8
A77-B4-C8
A1-B1-C9
A2-B1-C9
A3-B1-C9
A4-B1-C9
A5-B1-C9
A6-B1-C9
A7-B1-C9
A8-B1-C9
A9-B1-C9
A10-B1-C9
A11-B1-C9
A12-B1-C9
A13-B1-C9
A14-B1-C9
A15-B1-C9
A16-B1-C9
A17-B1-C9
A18-B1-C9
A19-B1-C9
A20-B1-C9
A21-B1-C9
A22-B1-C9
A23-B1-C9
A24-B1-C9
A25-B1-C9
A26-B1-C9
A27-B1-C9
A28-B1-C9
A29-B1-C9
A30-B1-C9
A31-B1-C9
A32-B1-C9
A33-B1-C9
A34-B1-C9
A35-B1-C9
A36-B1-C9
A37-B1-C9
A38-B1-C9
A39-B1-C9
A40-B1-C9
A41-B1-C9
A42-B1-C9
A43-B1-C9
A44-B1-C9
A45-B1-C9
A46-B1-C9
A47-B1-C9
A48-B1-C9
A49-B1-C9
A50-B1-C9
A51-B1-C9
A52-B1-C9
A53-B1-C9
A54-B1-C9
A55-B1-C9
A56-B1-C9
A57-B1-C9
A58-B1-C9
A59-B1-C9
A60-B1-C9
A61-B1-C9
A62-B1-C9
A63-B1-C9
A64-B1-C9
A65-B1-C9
A66-B1-C9
A67-B1-C9
A68-B1-C9
A69-B1-C9
A70-B1-C9
A71-B1-C9
A72-B1-C9
A73-B1-C9
A74-B1-C9
A75-B1-C9
A76-B1-C9
A77-B1-C9
A1-B2-C9
A2-B2-C9
A3-B2-C9
A4-B2-C9
A5-B2-C9
A6-B2-C9
A7-B2-C9
A8-B2-C9
A9-B2-C9
A10-B2-C9
A11-B2-C9
A12-B2-C9
A13-B2-C9
A14-B2-C9
A15-B2-C9
A16-B2-C9
A17-B2-C9
A18-B2-C9
A19-B2-C9
A20-B2-C9
A21-B2-C9
A22-B2-C9
A23-B2-C9
A24-B2-C9
A25-B2-C9
A26-B2-C9
A27-B2-C9
A28-B2-C9
A29-B2-C9
A30-B2-C9
A31-B2-C9
A32-B2-C9
A33-B2-C9
A34-B2-C9
A35-B2-C9
A36-B2-C9
A37-B2-C9
A38-B2-C9
A39-B2-C9
A40-B2-C9
A41-B2-C9
A42-B2-C9
A43-B2-C9
A44-B2-C9
A45-B2-C9
A46-B2-C9
A47-B2-C9
A48-B2-C9
A49-B2-C9
A50-B2-C9
A51-B2-C9
A52-B2-C9
A53-B2-C9
A54-B2-C9
A55-B2-C9
A56-B2-C9
A57-B2-C9
A58-B2-C9
A59-B2-C9
A60-B2-C9
A61-B2-C9
A62-B2-C9
A63-B2-C9
A64-B2-C9
A65-B2-C9
A66-B2-C9
A67-B2-C9
A68-B2-C9
A69-B2-C9
A70-B2-C9
A71-B2-C9
A72-B2-C9
A73-B2-C9
A74-B2-C9
A75-B2-C9
A76-B2-C9
A77-B2-C9
A1-B3-C9
A2-B3-C9
A3-B3-C9
A4-B3-C9
A5-B3-C9
A6-B3-C9
A7-B3-C9
A8-B3-C9
A9-B3-C9
A10-B3-C9
A11-B3-C9
A12-B3-C9
A13-B3-C9
A14-B3-C9
A15-B3-C9
A16-B3-C9
A17-B3-C9
A18-B3-C9
A19-B3-C9
A20-B3-C9
A21-B3-C9
A22-B3-C9
A23-B3-C9
A24-B3-C9
A25-B3-C9
A26-B3-C9
A27-B3-C9
A28-B3-C9
A29-B3-C9
A30-B3-C9
A31-B3-C9
A32-B3-C9
A33-B3-C9
A34-B3-C9
A35-B3-C9
A36-B3-C9
A37-B3-C9
A38-B3-C9
A39-B3-C9
A40-B3-C9
A41-B3-C9
A42-B3-C9
A43-B3-C9
A44-B3-C9
A45-B3-C9
A46-B3-C9
A47-B3-C9
A48-B3-C9
A49-B3-C9
A50-B3-C9
A51-B3-C9
A52-B3-C9
A53-B3-C9
A54-B3-C9
A55-B3-C9
A56-B3-C9
A57-B3-C9
A58-B3-C9
A59-B3-C9
A60-B3-C9
A61-B3-C9
A62-B3-C9
A63-B3-C9
A64-B3-C9
A65-B3-C9
A66-B3-C9
A67-B3-C9
A68-B3-C9
A69-B3-C9
A70-B3-C9
A71-B3-C9
A72-B3-C9
A73-B3-C9
A74-B3-C9
A75-B3-C9
A76-B3-C9
A77-B3-C9
A1-B4-C9
A2-B4-C9
A3-B4-C9
A4-B4-C9
A5-B4-C9
A6-B4-C9
A7-B4-C9
A8-B4-C9
A9-B4-C9
A10-B4-C9
A11-B4-C9
A12-B4-C9
A13-B4-C9

A14-B4-C9
A15-B4-C9
A16-B4-C9
A17-B4-C9
A18-B4-C9
A19-B4-C9
A20-B4-C9
A21-B4-C9
A22-B4-C9
A23-B4-C9
A24-B4-C9
A25-B4-C9
A26-B4-C9
A27-B4-C9
A28-B4-C9
A29-B4-C9
A30-B4-C9
A31-B4-C9
A32-B4-C9
A33-B4-C9
A34-B4-C9
A35-B4-C9
A36-B4-C9
A37-B4-C9
A38-B4-C9
A39-B4-C9
A40-B4-C9
A41-B4-C9
A42-B4-C9
A43-B4-C9
A44-B4-C9
A45-B4-C9
A46-B4-C9
A47-B4-C9
A48-B4-C9
A49-B4-C9
A50-B4-C9
A51-B4-C9
A52-B4-C9
A53-B4-C9
A54-B4-C9
A55-B4-C9
A56-B4-C9
A57-B4-C9
A58-B4-C9
A59-B4-C9
A60-B4-C9
A61-B4-C9
A62-B4-C9
A63-B4-C9
A64-B4-C9
A65-B4-C9
A66-B4-C9
A67-B4-C9
A68-B4-C9
A69-B4-C9
A70-B4-C9
A71-B4-C9
A72-B4-C9
A73-B4-C9
A74-B4-C9
A75-B4-C9
A76-B4-C9
A77-B4-C9
A1-B1-C10
A2-B1-C10
A3-B1-C10
A4-B1-C10
A5-B1-C10
A6-B1-C10
A7-B1-C10
A8-B1-C10
A9-B1-C10
A10-B1-C10
A11-B1-C10
A12-B1-C10
A13-B1-C10
A14-B1-C10
A15-B1-C10
A16-B1-C10
A17-B1-C10
A18-B1-C10
A19-B1-C10
A20-B1-C10
A21-B1-C10
A22-B1-C10
A23-B1-C10
A24-B1-C10
A25-B1-C10
A26-B1-C10
A27-B1-C10
A28-B1-C10
A29-B1-C10
A30-B1-C10
A31-B1-C10
A32-B1-C10
A33-B1-C10
A34-B1-C10
A35-B1-C10
A36-B1-C10
A37-B1-C10
A38-B1-C10
A39-B1-C10
A40-B1-C10
A41-B1-C10
A42-B1-C10
A43-B1-C10
A44-B1-C10
A45-B1-C10
A46-B1-C10
A47-B1-C10
A48-B1-C10
A49-B1-C10
A50-B1-C10
A51-B1-C10
A52-B1-C10
A53-B1-C10
A54-B1-C10
A55-B1-C10
A56-B1-C10
A57-B1-C10
A58-B1-C10
A59-B1-C10
A60-B1-C10
A61-B1-C10
A62-B1-C10
A63-B1-C10
A64-B1-C10
A65-B1-C10
A66-B1-C10
A67-B1-C10
A68-B1-C10
A69-B1-C10
A70-B1-C10
A71-B1-C10
A72-B1-C10
A73-B1-C10
A74-B1-C10
A75-B1-C10
A76-B1-C10
A77-B1-C10
A1-B2-C10
A2-B2-C10
A3-B2-C10
A4-B2-C10
A5-B2-C10
A6-B2-C10
A7-B2-C10
A8-B2-C10
A9-B2-C10
A10-B2-C10
A11-B2-C10
A12-B2-C10
A13-B2-C10
A14-B2-C10
A15-B2-C10
A16-B2-C10
A17-B2-C10
A18-B2-C10
A19-B2-C10
A20-B2-C10
A21-B2-C10
A22-B2-C10
A23-B2-C10
A24-B2-C10
A25-B2-C10
A26-B2-C10
A27-B2-C10
A28-B2-C10
A29-B2-C10
A30-B2-C10
A31-B2-C10
A32-B2-C10
A33-B2-C10
A34-B2-C10
A35-B2-C10
A36-B2-C10
A37-B2-C10
A38-B2-C10
A39-B2-C10
A40-B2-C10
A41-B2-C10
A42-B2-C10
A43-B2-C10
A44-B2-C10
A45-B2-C10
A46-B2-C10
A47-B2-C10
A48-B2-C10
A49-B2-C10
A50-B2-C10
A51-B2-C10
A52-B2-C10
A53-B2-C10
A54-B2-C10
A55-B2-C10
A56-B2-C10
A57-B2-C10
A58-B2-C10
A59-B2-C10
A60-B2-C10
A61-B2-C10
A62-B2-C10
A63-B2-C10
A64-B2-C10
A65-B2-C10
A66-B2-C10
A67-B2-C10
A68-B2-C10
A69-B2-C10
A70-B2-C10
A71-B2-C10
A72-B2-C10
A73-B2-C10
A74-B2-C10
A75-B2-C10
A76-B2-C10
A77-B2-C10
A1-B3-C10
A2-B3-C10
A3-B3-C10
A4-B3-C10
A5-B3-C10
A6-B3-C10
A7-B3-C10
A8-B3-C10
A9-B3-C10
A10-B3-C10
A11-B3-C10
A12-B3-C10
A13-B3-C10
A14-B3-C10
A15-B3-C10
A16-B3-C10
A17-B3-C10
A18-B3-C10
A19-B3-C10
A20-B3-C10
A21-B3-C10
A22-B3-C10
A23-B3-C10
A24-B3-C10
A25-B3-C10
A26-B3-C10
A27-B3-C10
A28-B3-C10
A29-B3-C10
A30-B3-C10
A31-B3-C10
A32-B3-C10
A33-B3-C10
A34-B3-C10
A35-B3-C10
A36-B3-C10
A37-B3-C10
A38-B3-C10
A39-B3-C10
A40-B3-C10
A41-B3-C10
A42-B3-C10
A43-B3-C10
A44-B3-C10
A45-B3-C10
A46-B3-C10

A47-B3-C10
A48-B3-C10
A49-B3-C10
A50-B3-C10
A51-B3-C10
A52-B3-C10
A53-B3-C10
A54-B3-C10
A55-B3-C10
A56-B3-C10
A57-B3-C10
A58-B3-C10
A59-B3-C10
A60-B3-C10
A61-B3-C10
A62-B3-C10
A63-B3-C10
A64-B3-C10
A65-B3-C10
A66-B3-C10
A67-B3-C10
A68-B3-C10
A69-B3-C10
A70-B3-C10
A71-B3-C10
A72-B3-C10
A73-B3-C10
A74-B3-C10
A75-B3-C10
A76-B3-C10
A77-B3-C10
A1-B4-C10
A2-B4-C10
A3-B4-C10
A4-B4-C10
A5-B4-C10
A6-B4-C10
A7-B4-C10
A8-B4-C10
A9-B4-C10
A10-B4-C10
A11-B4-C10
A12-B4-C10
A13-B4-C10
A14-B4-C10
A15-B4-C10
A16-B4-C10
A17-B4-C10
A18-B4-C10
A19-B4-C10
A20-B4-C10
A21-B4-C10
A22-B4-C10
A23-B4-C10
A24-B4-C10
A25-B4-C10
A26-B4-C10
A27-B4-C10
A28-B4-C10
A29-B4-C10
A30-B4-C10
A31-B4-C10
A32-B4-C10
A33-B4-C10
A34-B4-C10
A35-B4-C10
A36-B4-C10
A37-B4-C10
A38-B4-C10
A39-B4-C10
A40-B4-C10
A41-B4-C10
A42-B4-C10
A43-B4-C10
A44-B4-C10
A45-B4-C10
A46-B4-C10
A47-B4-C10
A48-B4-C10
A49-B4-C10
A50-B4-C10
A51-B4-C10
A52-B4-C10
A53-B4-C10
A54-B4-C10
A55-B4-C10
A56-B4-C10
A57-B4-C10
A58-B4-C10
A59-B4-C10
A60-B4-C10
A61-B4-C10
A62-B4-C10
A63-B4-C10
A64-B4-C10
A65-B4-C10
A66-B4-C10
A67-B4-C10
A68-B4-C10
A69-B4-C10
A70-B4-C10
A71-B4-C10
A72-B4-C10
A73-B4-C10
A74-B4-C10
A75-B4-C10
A76-B4-C10
A77-B4-C10
A1-B1-C11
A2-B1-C11
A3-B1-C11
A4-B1-C11
A5-B1-C11
A6-B1-C11
A7-B1-C11
A8-B1-C11
A9-B1-C11
A10-B1-C11
A11-B1-C11
A12-B1-C11
A13-B1-C11
A14-B1-C11
A15-B1-C11
A16-B1-C11
A17-B1-C11
A18-B1-C11
A19-B1-C11
A20-B1-C11
A21-B1-C11
A22-B1-C11
A23-B1-C11
A24-B1-C11
A25-B1-C11
A26-B1-C11
A27-B1-C11
A28-B1-C11
A29-B1-C11
A30-B1-C11
A31-B1-C11
A32-B1-C11
A33-B1-C11
A34-B1-C11
A35-B1-C11
A36-B1-C11
A37-B1-C11
A38-B1-C11
A39-B1-C11
A40-B1-C11
A41-B1-C11
A42-B1-C11
A43-B1-C11
A44-B1-C11
A45-B1-C11
A46-B1-C11
A47-B1-C11
A48-B1-C11
A49-B1-C11
A50-B1-C11
A51-B1-C11
A52-B1-C11
A53-B1-C11
A54-B1-C11
A55-B1-C11
A56-B1-C11
A57-B1-C11
A58-B1-C11
A59-B1-C11
A60-B1-C11
A61-B1-C11
A62-B1-C11
A63-B1-C11
A64-B1-C11
A65-B1-C11
A66-B1-C11
A67-B1-C11
A68-B1-C11
A69-B1-C11
A70-B1-C11
A71-B1-C11
A72-B1-C11
A73-B1-C11
A74-B1-C11
A75-B1-C11
A76-B1-C11
A77-B1-C11
A1-B2-C11
A2-B2-C11
A3-B2-C11
A4-B2-C11
A5-B2-C11
A6-B2-C11
A7-B2-C11
A8-B2-C11
A9-B2-C11
A10-B2-C11
A11-B2-C11
A12-B2-C11
A13-B2-C11
A14-B2-C11
A15-B2-C11
A16-B2-C11
A17-B2-C11
A18-B2-C11
A19-B2-C11
A20-B2-C11
A21-B2-C11
A22-B2-C11
A23-B2-C11
A24-B2-C11
A25-B2-C11
A26-B2-C11
A27-B2-C11
A28-B2-C11
A29-B2-C11
A30-B2-C11
A31-B2-C11
A32-B2-C11
A33-B2-C11
A34-B2-C11
A35-B2-C11
A36-B2-C11
A37-B2-C11
A38-B2-C11
A39-B2-C11
A40-B2-C11
A41-B2-C11
A42-B2-C11
A43-B2-C11
A44-B2-C11
A45-B2-C11
A46-B2-C11
A47-B2-C11
A48-B2-C11
A49-B2-C11
A50-B2-C11
A51-B2-C11
A52-B2-C11
A53-B2-C11
A54-B2-C11
A55-B2-C11
A56-B2-C11
A57-B2-C11
A58-B2-C11
A59-B2-C11
A60-B2-C11
A61-B2-C11
A62-B2-C11
A63-B2-C11
A64-B2-C11
A65-B2-C11
A66-B2-C11
A67-B2-C11
A68-B2-C11
A69-B2-C11
A70-B2-C11
A71-B2-C11
A72-B2-C11
A73-B2-C11
A74-B2-C11
A75-B2-C11
A76-B2-C11
A77-B2-C11
A1-B3-C11
A2-B3-C11

A3-B3-C11
A4-B3-C11
A5-B3-C11
A6-B3-C11
A7-B3-C11
A8-B3-C11
A9-B3-C11
A10-B3-C11
A11-B3-C11
A12-B3-C11
A13-B3-C11
A14-B3-C11
A15-B3-C11
A16-B3-C11
A17-B3-C11
A18-B3-C11
A19-B3-C11
A20-B3-C11
A21-B3-C11
A22-B3-C11
A23-B3-C11
A24-B3-C11
A25-B3-C11
A26-B3-C11
A27-B3-C11
A28-B3-C11
A29-B3-C11
A30-B3-C11
A31-B3-C11
A32-B3-C11
A33-B3-C11
A34-B3-C11
A35-B3-C11
A36-B3-C11
A37-B3-C11
A38-B3-C11
A39-B3-C11
A40-B3-C11
A41-B3-C11
A42-B3-C11
A43-B3-C11
A44-B3-C11
A45-B3-C11
A46-B3-C11
A47-B3-C11
A48-B3-C11
A49-B3-C11
A50-B3-C11
A51-B3-C11
A52-B3-C11
A53-B3-C11
A54-B3-C11
A55-B3-C11
A56-B3-C11
A57-B3-C11
A58-B3-C11
A59-B3-C11
A60-B3-C11
A61-B3-C11
A62-B3-C11
A63-B3-C11
A64-B3-C11
A65-B3-C11
A66-B3-C11
A67-B3-C11
A68-B3-C11
A69-B3-C11
A70-B3-C11
A71-B3-C11
A72-B3-C11
A73-B3-C11
A74-B3-C11
A75-B3-C11
A76-B3-C11
A77-B3-C11
A1-B4-C11
A2-B4-C11
A3-B4-C11
A4-B4-C11
A5-B4-C11
A6-B4-C11
A7-B4-C11
A8-B4-C11
A9-B4-C11
A10-B4-C11
A11-B4-C11
A12-B4-C11
A13-B4-C11
A14-B4-C11
A15-B4-C11
A16-B4-C11
A17-B4-C11
A18-B4-C11
A19-B4-C11
A20-B4-C11
A21-B4-C11
A22-B4-C11
A23-B4-C11
A24-B4-C11
A25-B4-C11
A26-B4-C11
A27-B4-C11
A28-B4-C11
A29-B4-C11
A30-B4-C11
A31-B4-C11
A32-B4-C11
A33-B4-C11
A34-B4-C11
A35-B4-C11
A36-B4-C11
A37-B4-C11
A38-B4-C11
A39-B4-C11
A40-B4-C11
A41-B4-C11
A42-B4-C11
A43-B4-C11
A44-B4-C11
A45-B4-C11
A46-B4-C11
A47-B4-C11
A48-B4-C11
A49-B4-C11
A50-B4-C11
A51-B4-C11
A52-B4-C11
A53-B4-C11
A54-B4-C11
A55-B4-C11
A56-B4-C11
A57-B4-C11
A58-B4-C11
A59-B4-C11
A60-B4-C11
A61-B4-C11
A62-B4-C11
A63-B4-C11
A64-B4-C11
A65-B4-C11
A66-B4-C11
A67-B4-C11
A68-B4-C11
A69-B4-C11
A70-B4-C11
A71-B4-C11
A72-B4-C11
A73-B4-C11
A74-B4-C11
A75-B4-C11
A76-B4-C11
A77-B4-C11
A1-B1-C12
A2-B1-C12
A3-B1-C12
A4-B1-C12
A5-B1-C12
A6-B1-C12
A7-B1-C12
A8-B1-C12
A9-B1-C12
A10-B1-C12
A11-B1-C12
A12-B1-C12
A13-B1-C12
A14-B1-C12
A15-B1-C12
A16-B1-C12
A17-B1-C12
A18-B1-C12
A19-B1-C12
A20-B1-C12
A21-B1-C12
A22-B1-C12
A23-B1-C12
A24-B1-C12
A25-B1-C12
A26-B1-C12
A27-B1-C12
A28-B1-C12
A29-B1-C12
A30-B1-C12
A31-B1-C12
A32-B1-C12
A33-B1-C12
A34-B1-C12
A35-B1-C12
A36-B1-C12
A37-B1-C12
A38-B1-C12
A39-B1-C12
A40-B1-C12
A41-B1-C12
A42-B1-C12
A43-B1-C12
A44-B1-C12
A45-B1-C12
A46-B1-C12
A47-B1-C12
A48-B1-C12
A49-B1-C12
A50-B1-C12
A51-B1-C12
A52-B1-C12
A53-B1-C12
A54-B1-C12
A55-B1-C12
A56-B1-C12
A57-B1-C12
A58-B1-C12
A59-B1-C12
A60-B1-C12
A61-B1-C12
A62-B1-C12
A63-B1-C12
A64-B1-C12
A65-B1-C12
A66-B1-C12
A67-B1-C12
A68-B1-C12
A69-B1-C12
A70-B1-C12
A71-B1-C12
A72-B1-C12
A73-B1-C12
A74-B1-C12
A75-B1-C12
A76-B1-C12
A77-B1-C12
A1-B2-C12
A2-B2-C12
A3-B2-C12
A4-B2-C12
A5-B2-C12
A6-B2-C12
A7-B2-C12
A8-B2-C12
A9-B2-C12
A10-B2-C12
A11-B2-C12
A12-B2-C12
A13-B2-C12
A14-B2-C12
A15-B2-C12
A16-B2-C12
A17-B2-C12
A18-B2-C12
A19-B2-C12
A20-B2-C12
A21-B2-C12
A22-B2-C12
A23-B2-C12
A24-B2-C12
A25-B2-C12
A26-B2-C12
A27-B2-C12
A28-B2-C12
A29-B2-C12
A30-B2-C12
A31-B2-C12
A32-B2-C12
A33-B2-C12
A34-B2-C12
A35-B2-C12

A36-B2-C12
A37-B2-C12
A38-B2-C12
A39-B2-C12
A40-B2-C12
A41-B2-C12
A42-B2-C12
A43-B2-C12
A44-B2-C12
A45-B2-C12
A46-B2-C12
A47-B2-C12
A48-B2-C12
A49-B2-C12
A50-B2-C12
A51-B2-C12
A52-B2-C12
A53-B2-C12
A54-B2-C12
A55-B2-C12
A56-B2-C12
A57-B2-C12
A58-B2-C12
A59-B2-C12
A60-B2-C12
A61-B2-C12
A62-B2-C12
A63-B2-C12
A64-B2-C12
A65-B2-C12
A66-B2-C12
A67-B2-C12
A68-B2-C12
A69-B2-C12
A70-B2-C12
A71-B2-C12
A72-B2-C12
A73-B2-C12
A74-B2-C12
A75-B2-C12
A76-B2-C12
A77-B2-C12
A1-B3-C12
A2-B3-C12
A3-B3-C12
A4-B3-C12
A5-B3-C12
A6-B3-C12
A7-B3-C12
A8-B3-C12
A9-B3-C12
A10-B3-C12
A11-B3-C12
A12-B3-C12
A13-B3-C12
A14-B3-C12
A15-B3-C12
A16-B3-C12
A17-B3-C12
A18-B3-C12
A19-B3-C12
A20-B3-C12
A21-B3-C12
A22-B3-C12
A23-B3-C12
A24-B3-C12
A25-B3-C12
A26-B3-C12
A27-B3-C12
A28-B3-C12
A29-B3-C12
A30-B3-C12
A31-B3-C12
A32-B3-C12
A33-B3-C12
A34-B3-C12
A35-B3-C12
A36-B3-C12
A37-B3-C12
A38-B3-C12
A39-B3-C12
A40-B3-C12
A41-B3-C12
A42-B3-C12
A43-B3-C12
A44-B3-C12
A45-B3-C12
A46-B3-C12
A47-B3-C12
A48-B3-C12
A49-B3-C12
A50-B3-C12
A51-B3-C12
A52-B3-C12
A53-B3-C12
A54-B3-C12
A55-B3-C12
A56-B3-C12
A57-B3-C12
A58-B3-C12
A59-B3-C12
A60-B3-C12
A61-B3-C12
A62-B3-C12
A63-B3-C12
A64-B3-C12
A65-B3-C12
A66-B3-C12
A67-B3-C12
A68-B3-C12
A69-B3-C12
A70-B3-C12
A71-B3-C12
A72-B3-C12
A73-B3-C12
A74-B3-C12
A75-B3-C12
A76-B3-C12
A77-B3-C12
A1-B4-C12
A2-B4-C12
A3-B4-C12
A4-B4-C12
A5-B4-C12
A6-B4-C12
A7-B4-C12
A8-B4-C12
A9-B4-C12
A10-B4-C12
A11-B4-C12
A12-B4-C12
A13-B4-C12
A14-B4-C12
A15-B4-C12
A16-B4-C12
A17-B4-C12
A18-B4-C12
A19-B4-C12
A20-B4-C12
A21-B4-C12
A22-B4-C12
A23-B4-C12
A24-B4-C12
A25-B4-C12
A26-B4-C12
A27-B4-C12
A28-B4-C12
A29-B4-C12
A30-B4-C12
A31-B4-C12
A32-B4-C12
A33-B4-C12
A34-B4-C12
A35-B4-C12
A36-B4-C12
A37-B4-C12
A38-B4-C12
A39-B4-C12
A40-B4-C12
A41-B4-C12
A42-B4-C12
A43-B4-C12
A44-B4-C12
A45-B4-C12
A46-B4-C12
A47-B4-C12
A48-B4-C12
A49-B4-C12
A50-B4-C12
A51-B4-C12
A52-B4-C12
A53-B4-C12
A54-B4-C12
A55-B4-C12
A56-B4-C12
A57-B4-C12
A58-B4-C12
A59-B4-C12
A60-B4-C12
A61-B4-C12
A62-B4-C12
A63-B4-C12
A64-B4-C12
A65-B4-C12
A66-B4-C12
A67-B4-C12
A68-B4-C12
A69-B4-C12
A70-B4-C12
A71-B4-C12
A72-B4-C12
A73-B4-C12
A74-B4-C12
A75-B4-C12
A76-B4-C12
A77-B4-C12
A1-B1-C13
A2-B1-C13
A3-B1-C13
A4-B1-C13
A5-B1-C13
A6-B1-C13
A7-B1-C13
A8-B1-C13
A9-B1-C13
A10-B1-C13
A11-B1-C13
A12-B1-C13
A13-B1-C13
A14-B1-C13
A15-B1-C13
A16-B1-C13
A17-B1-C13
A18-B1-C13
A19-B1-C13
A20-B1-C13
A21-B1-C13
A22-B1-C13
A23-B1-C13
A24-B1-C13
A25-B1-C13
A26-B1-C13
A27-B1-C13
A28-B1-C13
A29-B1-C13
A30-B1-C13
A31-B1-C13
A32-B1-C13
A33-B1-C13
A34-B1-C13
A35-B1-C13
A36-B1-C13
A37-B1-C13
A38-B1-C13
A39-B1-C13
A40-B1-C13
A41-B1-C13
A42-B1-C13
A43-B1-C13
A44-B1-C13
A45-B1-C13
A46-B1-C13
A47-B1-C13
A48-B1-C13
A49-B1-C13
A50-B1-C13
A51-B1-C13
A52-B1-C13
A53-B1-C13
A54-B1-C13
A55-B1-C13
A56-B1-C13
A57-B1-C13
A58-B1-C13
A59-B1-C13
A60-B1-C13
A61-B1-C13
A62-B1-C13
A63-B1-C13
A64-B1-C13
A65-B1-C13
A66-B1-C13
A67-B1-C13
A68-B1-C13

A69-B1-C13
A70-B1-C13
A71-B1-C13
A72-B1-C13
A73-B1-C13
A74-B1-C13
A75-B1-C13
A76-B1-C13
A77-B1-C13
A1-B2-C13
A2-B2-C13
A3-B2-C13
A4-B2-C13
A5-B2-C13
A6-B2-C13
A7-B2-C13
A8-B2-C13
A9-B2-C13
A10-B2-C13
A11-B2-C13
A12-B2-C13
A13-B2-C13
A14-B2-C13
A15-B2-C13
A16-B2-C13
A17-B2-C13
A18-B2-C13
A19-B2-C13
A20-B2-C13
A21-B2-C13
A22-B2-C13
A23-B2-C13
A24-B2-C13
A25-B2-C13
A26-B2-C13
A27-B2-C13
A28-B2-C13
A29-B2-C13
A30-B2-C13
A31-B2-C13
A32-B2-C13
A33-B2-C13
A34-B2-C13
A35-B2-C13
A36-B2-C13
A37-B2-C13
A38-B2-C13
A39-B2-C13
A40-B2-C13
A41-B2-C13
A42-B2-C13
A43-B2-C13
A44-B2-C13
A45-B2-C13
A46-B2-C13
A47-B2-C13
A48-B2-C13
A49-B2-C13
A50-B2-C13
A51-B2-C13
A52-B2-C13
A53-B2-C13
A54-B2-C13
A55-B2-C13
A56-B2-C13
A57-B2-C13
A58-B2-C13
A59-B2-C13
A60-B2-C13
A61-B2-C13
A62-B2-C13
A63-B2-C13
A64-B2-C13
A65-B2-C13
A66-B2-C13
A67-B2-C13
A68-B2-C13
A69-B2-C13
A70-B2-C13
A71-B2-C13
A72-B2-C13
A73-B2-C13
A74-B2-C13
A75-B2-C13
A76-B2-C13
A77-B2-C13
A1-B3-C13
A2-B3-C13
A3-B3-C13
A4-B3-C13
A5-B3-C13
A6-B3-C13
A7-B3-C13
A8-B3-C13
A9-B3-C13
A10-B3-C13
A11-B3-C13
A12-B3-C13
A13-B3-C13
A14-B3-C13
A15-B3-C13
A16-B3-C13
A17-B3-C13
A18-B3-C13
A19-B3-C13
A20-B3-C13
A21-B3-C13
A22-B3-C13
A23-B3-C13
A24-B3-C13
A25-B3-C13
A26-B3-C13
A27-B3-C13
A28-B3-C13
A29-B3-C13
A30-B3-C13
A31-B3-C13
A32-B3-C13
A33-B3-C13
A34-B3-C13
A35-B3-C13
A36-B3-C13
A37-B3-C13
A38-B3-C13
A39-B3-C13
A40-B3-C13
A41-B3-C13
A42-B3-C13
A43-B3-C13
A44-B3-C13
A45-B3-C13
A46-B3-C13
A47-B3-C13
A48-B3-C13
A49-B3-C13
A50-B3-C13
A51-B3-C13
A52-B3-C13
A53-B3-C13
A54-B3-C13
A55-B3-C13
A56-B3-C13
A57-B3-C13
A58-B3-C13
A59-B3-C13
A60-B3-C13
A61-B3-C13
A62-B3-C13
A63-B3-C13
A64-B3-C13
A65-B3-C13
A66-B3-C13
A67-B3-C13
A68-B3-C13
A69-B3-C13
A70-B3-C13
A71-B3-C13
A72-B3-C13
A73-B3-C13
A74-B3-C13
A75-B3-C13
A76-B3-C13
A77-B3-C13
A1-B4-C13
A2-B4-C13
A3-B4-C13
A4-B4-C13
A5-B4-C13
A6-B4-C13
A7-B4-C13
A8-B4-C13
A9-B4-C13
A10-B4-C13
A11-B4-C13
A12-B4-C13
A13-B4-C13
A14-B4-C13
A15-B4-C13
A16-B4-C13
A17-B4-C13
A18-B4-C13
A19-B4-C13
A20-B4-C13
A21-B4-C13
A22-B4-C13
A23-B4-C13
A24-B4-C13
A25-B4-C13
A26-B4-C13
A27-B4-C13
A28-B4-C13
A29-B4-C13
A30-B4-C13
A31-B4-C13
A32-B4-C13
A33-B4-C13
A34-B4-C13
A35-B4-C13
A36-B4-C13
A37-B4-C13
A38-B4-C13
A39-B4-C13
A40-B4-C13
A41-B4-C13
A42-B4-C13
A43-B4-C13
A44-B4-C13
A45-B4-C13
A46-B4-C13
A47-B4-C13
A48-B4-C13
A49-B4-C13
A50-B4-C13
A51-B4-C13
A52-B4-C13
A53-B4-C13
A54-B4-C13
A55-B4-C13
A56-B4-C13
A57-B4-C13
A58-B4-C13
A59-B4-C13
A60-B4-C13
A61-B4-C13
A62-B4-C13
A63-B4-C13
A64-B4-C13
A65-B4-C13
A66-B4-C13
A67-B4-C13
A68-B4-C13
A69-B4-C13
A70-B4-C13
A71-B4-C13
A72-B4-C13
A73-B4-C13
A74-B4-C13
A75-B4-C13
A76-B4-C13
A77-B4-C13
A1-B1-C14
A2-B1-C14
A3-B1-C14
A4-B1-C14
A5-B1-C14
A6-B1-C14
A7-B1-C14
A8-B1-C14
A9-B1-C14
A10-B1-C14
A11-B1-C14
A12-B1-C14
A13-B1-C14
A14-B1-C14
A15-B1-C14
A16-B1-C14
A17-B1-C14
A18-B1-C14
A19-B1-C14
A20-B1-C14
A21-B1-C14
A22-B1-C14
A23-B1-C14
A24-B1-C14

A25-B1-C14
A26-B1-C14
A27-B1-C14
A28-B1-C14
A29-B1-C14
A30-B1-C14
A31-B1-C14
A32-B1-C14
A33-B1-C14
A34-B1-C14
A35-B1-C14
A36-B1-C14
A37-B1-C14
A38-B1-C14
A39-B1-C14
A40-B1-C14
A41-B1-C14
A42-B1-C14
A43-B1-C14
A44-B1-C14
A45-B1-C14
A46-B1-C14
A47-B1-C14
A48-B1-C14
A49-B1-C14
A50-B1-C14
A51-B1-C14
A52-B1-C14
A53-B1-C14
A54-B1-C14
A55-B1-C14
A56-B1-C14
A57-B1-C14
A58-B1-C14
A59-B1-C14
A60-B1-C14
A61-B1-C14
A62-B1-C14
A63-B1-C14
A64-B1-C14
A65-B1-C14
A66-B1-C14
A67-B1-C14
A68-B1-C14
A69-B1-C14
A70-B1-C14
A71-B1-C14
A72-B1-C14
A73-B1-C14
A74-B1-C14
A75-B1-C14
A76-B1-C14
A77-B1-C14
A1-B2-C14
A2-B2-C14
A3-B2-C14
A4-B2-C14
A5-B2-C14
A6-B2-C14
A7-B2-C14
A8-B2-C14
A9-B2-C14
A10-B2-C14
A11-B2-C14
A12-B2-C14
A13-B2-C14
A14-B2-C14
A15-B2-C14
A16-B2-C14
A17-B2-C14
A18-B2-C14
A19-B2-C14
A20-B2-C14
A21-B2-C14
A22-B2-C14
A23-B2-C14
A24-B2-C14
A25-B2-C14
A26-B2-C14
A27-B2-C14
A28-B2-C14
A29-B2-C14
A30-B2-C14
A31-B2-C14
A32-B2-C14
A33-B2-C14
A34-B2-C14
A35-B2-C14
A36-B2-C14
A37-B2-C14
A38-B2-C14
A39-B2-C14
A40-B2-C14
A41-B2-C14
A42-B2-C14
A43-B2-C14
A44-B2-C14
A45-B2-C14
A46-B2-C14
A47-B2-C14
A48-B2-C14
A49-B2-C14
A50-B2-C14
A51-B2-C14
A52-B2-C14
A53-B2-C14
A54-B2-C14
A55-B2-C14
A56-B2-C14
A57-B2-C14
A58-B2-C14
A59-B2-C14
A60-B2-C14
A61-B2-C14
A62-B2-C14
A63-B2-C14
A64-B2-C14
A65-B2-C14
A66-B2-C14
A67-B2-C14
A68-B2-C14
A69-B2-C14
A70-B2-C14
A71-B2-C14
A72-B2-C14
A73-B2-C14
A74-B2-C14
A75-B2-C14
A76-B2-C14
A77-B2-C14
A1-B3-C14
A2-B3-C14
A3-B3-C14
A4-B3-C14
A5-B3-C14
A6-B3-C14
A7-B3-C14
A8-B3-C14
A9-B3-C14
A10-B3-C14
A11-B3-C14
A12-B3-C14
A13-B3-C14
A14-B3-C14
A15-B3-C14
A16-B3-C14
A17-B3-C14
A18-B3-C14
A19-B3-C14
A20-B3-C14
A21-B3-C14
A22-B3-C14
A23-B3-C14
A24-B3-C14
A25-B3-C14
A26-B3-C14
A27-B3-C14
A28-B3-C14
A29-B3-C14
A30-B3-C14
A31-B3-C14
A32-B3-C14
A33-B3-C14
A34-B3-C14
A35-B3-C14
A36-B3-C14
A37-B3-C14
A38-B3-C14
A39-B3-C14
A40-B3-C14
A41-B3-C14
A42-B3-C14
A43-B3-C14
A44-B3-C14
A45-B3-C14
A46-B3-C14
A47-B3-C14
A48-B3-C14
A49-B3-C14
A50-B3-C14
A51-B3-C14
A52-B3-C14
A53-B3-C14
A54-B3-C14
A55-B3-C14
A56-B3-C14
A57-B3-C14
A58-B3-C14
A59-B3-C14
A60-B3-C14
A61-B3-C14
A62-B3-C14
A63-B3-C14
A64-B3-C14
A65-B3-C14
A66-B3-C14
A67-B3-C14
A68-B3-C14
A69-B3-C14
A70-B3-C14
A71-B3-C14
A72-B3-C14
A73-B3-C14
A74-B3-C14
A75-B3-C14
A76-B3-C14
A77-B3-C14
A1-B4-C14
A2-B4-C14
A3-B4-C14
A4-B4-C14
A5-B4-C14
A6-B4-C14
A7-B4-C14
A8-B4-C14
A9-B4-C14
A10-B4-C14
A11-B4-C14
A12-B4-C14
A13-B4-C14
A14-B4-C14
A15-B4-C14
A16-B4-C14
A17-B4-C14
A18-B4-C14
A19-B4-C14
A20-B4-C14
A21-B4-C14
A22-B4-C14
A23-B4-C14
A24-B4-C14
A25-B4-C14
A26-B4-C14
A27-B4-C14
A28-B4-C14
A29-B4-C14
A30-B4-C14
A31-B4-C14
A32-B4-C14
A33-B4-C14
A34-B4-C14
A35-B4-C14
A36-B4-C14
A37-B4-C14
A38-B4-C14
A39-B4-C14
A40-B4-C14
A41-B4-C14
A42-B4-C14
A43-B4-C14
A44-B4-C14
A45-B4-C14
A46-B4-C14
A47-B4-C14
A48-B4-C14
A49-B4-C14
A50-B4-C14
A51-B4-C14
A52-B4-C14
A53-B4-C14
A54-B4-C14
A55-B4-C14
A56-B4-C14
A57-B4-C14

A58-B4-C14
A59-B4-C14
A60-B4-C14
A61-B4-C14
A62-B4-C14
A63-B4-C14
A64-B4-C14
A65-B4-C14
A66-B4-C14
A67-B4-C14
A68-B4-C14
A69-B4-C14
A70-B4-C14
A71-B4-C14
A72-B4-C14
A73-B4-C14
A74-B4-C14
A75-B4-C14
A76-B4-C14
A77-B4-C14
A1-B1-C15
A2-B1-C15
A3-B1-C15
A4-B1-C15
A5-B1-C15
A6-B1-C15
A7-B1-C15
A8-B1-C15
A9-B1-C15
A10-B1-C15
A11-B1-C15
A12-B1-C15
A13-B1-C15
A14-B1-C15
A15-B1-C15
A16-B1-C15
A17-B1-C15
A18-B1-C15
A19-B1-C15
A20-B1-C15
A21-B1-C15
A22-B1-C15
A23-B1-C15
A24-B1-C15
A25-B1-C15
A26-B1-C15
A27-B1-C15
A28-B1-C15
A29-B1-C15
A30-B1-C15
A31-B1-C15
A32-B1-C15
A33-B1-C15
A34-B1-C15
A35-B1-C15
A36-B1-C15
A37-B1-C15
A38-B1-C15
A39-B1-C15
A40-B1-C15
A41-B1-C15
A42-B1-C15
A43-B1-C15
A44-B1-C15
A45-B1-C15
A46-B1-C15
A47-B1-C15
A48-B1-C15
A49-B1-C15
A50-B1-C15
A51-B1-C15
A52-B1-C15
A53-B1-C15
A54-B1-C15
A55-B1-C15
A56-B1-C15
A57-B1-C15
A58-B1-C15
A59-B1-C15
A60-B1-C15
A61-B1-C15
A62-B1-C15
A63-B1-C15
A64-B1-C15
A65-B1-C15
A66-B1-C15
A67-B1-C15
A68-B1-C15
A69-B1-C15
A70-B1-C15
A71-B1-C15
A72-B1-C15
A73-B1-C15
A74-B1-C15
A75-B1-C15
A76-B1-C15
A77-B1-C15
A1-B2-C15
A2-B2-C15
A3-B2-C15
A4-B2-C15
A5-B2-C15
A6-B2-C15
A7-B2-C15
A8-B2-C15
A9-B2-C15
A10-B2-C15
A11-B2-C15
A12-B2-C15
A13-B2-C15
A14-B2-C15
A15-B2-C15
A16-B2-C15
A17-B2-C15
A18-B2-C15
A19-B2-C15
A20-B2-C15
A21-B2-C15
A22-B2-C15
A23-B2-C15
A24-B2-C15
A25-B2-C15
A26-B2-C15
A27-B2-C15
A28-B2-C15
A29-B2-C15
A30-B2-C15
A31-B2-C15
A32-B2-C15
A33-B2-C15
A34-B2-C15
A35-B2-C15
A36-B2-C15
A37-B2-C15
A38-B2-C15
A39-B2-C15
A40-B2-C15
A41-B2-C15
A42-B2-C15
A43-B2-C15
A44-B2-C15
A45-B2-C15
A46-B2-C15
A47-B2-C15
A48-B2-C15
A49-B2-C15
A50-B2-C15
A51-B2-C15
A52-B2-C15
A53-B2-C15
A54-B2-C15
A55-B2-C15
A56-B2-C15
A57-B2-C15
A58-B2-C15
A59-B2-C15
A60-B2-C15
A61-B2-C15
A62-B2-C15
A63-B2-C15
A64-B2-C15
A65-B2-C15
A66-B2-C15
A67-B2-C15
A68-B2-C15
A69-B2-C15
A70-B2-C15
A71-B2-C15
A72-B2-C15
A73-B2-C15
A74-B2-C15
A75-B2-C15
A76-B2-C15
A77-B2-C15
A1-B3-C15
A2-B3-C15
A3-B3-C15
A4-B3-C15
A5-B3-C15
A6-B3-C15
A7-B3-C15
A8-B3-C15
A9-B3-C15
A10-B3-C15
A11-B3-C15
A12-B3-C15
A13-B3-C15
A14-B3-C15
A15-B3-C15
A16-B3-C15
A17-B3-C15
A18-B3-C15
A19-B3-C15
A20-B3-C15
A21-B3-C15
A22-B3-C15
A23-B3-C15
A24-B3-C15
A25-B3-C15
A26-B3-C15
A27-B3-C15
A28-B3-C15
A29-B3-C15
A30-B3-C15
A31-B3-C15
A32-B3-C15
A33-B3-C15
A34-B3-C15
A35-B3-C15
A36-B3-C15
A37-B3-C15
A38-B3-C15
A39-B3-C15
A40-B3-C15
A41-B3-C15
A42-B3-C15
A43-B3-C15
A44-B3-C15
A45-B3-C15
A46-B3-C15
A47-B3-C15
A48-B3-C15
A49-B3-C15
A50-B3-C15
A51-B3-C15
A52-B3-C15
A53-B3-C15
A54-B3-C15
A55-B3-C15
A56-B3-C15
A57-B3-C15
A58-B3-C15
A59-B3-C15
A60-B3-C15
A61-B3-C15
A62-B3-C15
A63-B3-C15
A64-B3-C15
A65-B3-C15
A66-B3-C15
A67-B3-C15
A68-B3-C15
A69-B3-C15
A70-B3-C15
A71-B3-C15
A72-B3-C15
A73-B3-C15
A74-B3-C15
A75-B3-C15
A76-B3-C15
A77-B3-C15
A1-B4-C15
A2-B4-C15
A3-B4-C15
A4-B4-C15
A5-B4-C15
A6-B4-C15
A7-B4-C15
A8-B4-C15
A9-B4-C15
A10-B4-C15
A11-B4-C15
A12-B4-C15
A13-B4-C15

A14-B4-C15
A15-B4-C15
A16-B4-C15
A17-B4-C15
A18-B4-C15
A19-B4-C15
A20-B4-C15
A21-B4-C15
A22-B4-C15
A23-B4-C15
A24-B4-C15
A25-B4-C15
A26-B4-C15
A27-B4-C15
A28-B4-C15
A29-B4-C15
A30-B4-C15
A31-B4-C15
A32-B4-C15
A33-B4-C15
A34-B4-C15
A35-B4-C15
A36-B4-C15
A37-B4-C15
A38-B4-C15
A39-B4-C15
A40-B4-C15
A41-B4-C15
A42-B4-C15
A43-B4-C15
A44-B4-C15
A45-B4-C15
A46-B4-C15
A47-B4-C15
A48-B4-C15
A49-B4-C15
A50-B4-C15
A51-B4-C15
A52-B4-C15
A53-B4-C15
A54-B4-C15
A55-B4-C15
A56-B4-C15
A57-B4-C15
A58-B4-C15
A59-B4-C15
A60-B4-C15
A61-B4-C15
A62-B4-C15
A63-B4-C15
A64-B4-C15
A65-B4-C15
A66-B4-C15
A67-B4-C15
A68-B4-C15
A69-B4-C15
A70-B4-C15
A71-B4-C15
A72-B4-C15
A73-B4-C15
A74-B4-C15
A75-B4-C15
A76-B4-C15
A77-B4-C15
A1-B1-C16
A2-B1-C16
A3-B1-C16
A4-B1-C16
A5-B1-C16
A6-B1-C16
A7-B1-C16
A8-B1-C16
A9-B1-C16
A10-B1-C16
A11-B1-C16
A12-B1-C16
A13-B1-C16
A14-B1-C16
A15-B1-C16
A16-B1-C16
A17-B1-C16
A18-B1-C16
A19-B1-C16
A20-B1-C16
A21-B1-C16
A22-B1-C16
A23-B1-C16
A24-B1-C16
A25-B1-C16
A26-B1-C16
A27-B1-C16
A28-B1-C16
A29-B1-C16
A30-B1-C16
A31-B1-C16
A32-B1-C16
A33-B1-C16
A34-B1-C16
A35-B1-C16
A36-B1-C16
A37-B1-C16
A38-B1-C16
A39-B1-C16
A40-B1-C16
A41-B1-C16
A42-B1-C16
A43-B1-C16
A44-B1-C16
A45-B1-C16
A46-B1-C16
A47-B1-C16
A48-B1-C16
A49-B1-C16
A50-B1-C16
A51-B1-C16
A52-B1-C16
A53-B1-C16
A54-B1-C16
A55-B1-C16
A56-B1-C16
A57-B1-C16
A58-B1-C16
A59-B1-C16
A60-B1-C16
A61-B1-C16
A62-B1-C16
A63-B1-C16
A64-B1-C16
A65-B1-C16
A66-B1-C16
A67-B1-C16
A68-B1-C16
A69-B1-C16
A70-B1-C16
A71-B1-C16
A72-B1-C16
A73-B1-C16
A74-B1-C16
A75-B1-C16
A76-B1-C16
A77-B1-C16
A1-B2-C16
A2-B2-C16
A3-B2-C16
A4-B2-C16
A5-B2-C16
A6-B2-C16
A7-B2-C16
A8-B2-C16
A9-B2-C16
A10-B2-C16
A11-B2-C16
A12-B2-C16
A13-B2-C16
A14-B2-C16
A15-B2-C16
A16-B2-C16
A17-B2-C16
A18-B2-C16
A19-B2-C16
A20-B2-C16
A21-B2-C16
A22-B2-C16
A23-B2-C16
A24-B2-C16
A25-B2-C16
A26-B2-C16
A27-B2-C16
A28-B2-C16
A29-B2-C16
A30-B2-C16
A31-B2-C16
A32-B2-C16
A33-B2-C16
A34-B2-C16
A35-B2-C16
A36-B2-C16
A37-B2-C16
A38-B2-C16
A39-B2-C16
A40-B2-C16
A41-B2-C16
A42-B2-C16
A43-B2-C16
A44-B2-C16
A45-B2-C16
A46-B2-C16
A47-B2-C16
A48-B2-C16
A49-B2-C16
A50-B2-C16
A51-B2-C16
A52-B2-C16
A53-B2-C16
A54-B2-C16
A55-B2-C16
A56-B2-C16
A57-B2-C16
A58-B2-C16
A59-B2-C16
A60-B2-C16
A61-B2-C16
A62-B2-C16
A63-B2-C16
A64-B2-C16
A65-B2-C16
A66-B2-C16
A67-B2-C16
A68-B2-C16
A69-B2-C16
A70-B2-C16
A71-B2-C16
A72-B2-C16
A73-B2-C16
A74-B2-C16
A75-B2-C16
A76-B2-C16
A77-B2-C16
A1-B3-C16
A2-B3-C16
A3-B3-C16
A4-B3-C16
A5-B3-C16
A6-B3-C16
A7-B3-C16
A8-B3-C16
A9-B3-C16
A10-B3-C16
A11-B3-C16
A12-B3-C16
A13-B3-C16
A14-B3-C16
A15-B3-C16
A16-B3-C16
A17-B3-C16
A18-B3-C16
A19-B3-C16
A20-B3-C16
A21-B3-C16
A22-B3-C16
A23-B3-C16
A24-B3-C16
A25-B3-C16
A26-B3-C16
A27-B3-C16
A28-B3-C16
A29-B3-C16
A30-B3-C16
A31-B3-C16
A32-B3-C16
A33-B3-C16
A34-B3-C16
A35-B3-C16
A36-B3-C16
A37-B3-C16
A38-B3-C16
A39-B3-C16
A40-B3-C16
A41-B3-C16
A42-B3-C16
A43-B3-C16
A44-B3-C16
A45-B3-C16
A46-B3-C16

A47-B3-C16
A48-B3-C16
A49-B3-C16
A50-B3-C16
A51-B3-C16
A52-B3-C16
A53-B3-C16
A54-B3-C16
A55-B3-C16
A56-B3-C16
A57-B3-C16
A58-B3-C16
A59-B3-C16
A60-B3-C16
A61-B3-C16
A62-B3-C16
A63-B3-C16
A64-B3-C16
A65-B3-C16
A66-B3-C16
A67-B3-C16
A68-B3-C16
A69-B3-C16
A70-B3-C16
A71-B3-C16
A72-B3-C16
A73-B3-C16
A74-B3-C16
A75-B3-C16
A76-B3-C16
A77-B3-C16
A1-B4-C16
A2-B4-C16
A3-B4-C16
A4-B4-C16
A5-B4-C16
A6-B4-C16
A7-B4-C16
A8-B4-C16
A9-B4-C16
A10-B4-C16
A11-B4-C16
A12-B4-C16
A13-B4-C16
A14-B4-C16
A15-B4-C16
A16-B4-C16
A17-B4-C16
A18-B4-C16
A19-B4-C16
A20-B4-C16
A21-B4-C16
A22-B4-C16
A23-B4-C16
A24-B4-C16
A25-B4-C16
A26-B4-C16
A27-B4-C16
A28-B4-C16
A29-B4-C16
A30-B4-C16
A31-B4-C16
A32-B4-C16
A33-B4-C16
A34-B4-C16
A35-B4-C16
A36-B4-C16
A37-B4-C16
A38-B4-C16
A39-B4-C16
A40-B4-C16
A41-B4-C16
A42-B4-C16
A43-B4-C16
A44-B4-C16
A45-B4-C16
A46-B4-C16
A47-B4-C16
A48-B4-C16
A49-B4-C16
A50-B4-C16
A51-B4-C16
A52-B4-C16
A53-B4-C16
A54-B4-C16
A55-B4-C16
A56-B4-C16
A57-B4-C16
A58-B4-C16
A59-B4-C16
A60-B4-C16
A61-B4-C16
A62-B4-C16
A63-B4-C16
A64-B4-C16
A65-B4-C16
A66-B4-C16
A67-B4-C16
A68-B4-C16
A69-B4-C16
A70-B4-C16
A71-B4-C16
A72-B4-C16
A73-B4-C16
A74-B4-C16
A75-B4-C16
A76-B4-C16
A77-B4-C16
A1-B1-C17
A2-B1-C17
A3-B1-C17
A4-B1-C17
A5-B1-C17
A6-B1-C17
A7-B1-C17
A8-B1-C17
A9-B1-C17
A10-B1-C17
A11-B1-C17
A12-B1-C17
A13-B1-C17
A14-B1-C17
A15-B1-C17
A16-B1-C17
A17-B1-C17
A18-B1-C17
A19-B1-C17
A20-B1-C17
A21-B1-C17
A22-B1-C17
A23-B1-C17
A24-B1-C17
A25-B1-C17
A26-B1-C17
A27-B1-C17
A28-B1-C17
A29-B1-C17
A30-B1-C17
A31-B1-C17
A32-B1-C17
A33-B1-C17
A34-B1-C17
A35-B1-C17
A36-B1-C17
A37-B1-C17
A38-B1-C17
A39-B1-C17
A40-B1-C17
A41-B1-C17
A42-B1-C17
A43-B1-C17
A44-B1-C17
A45-B1-C17
A46-B1-C17
A47-B1-C17
A48-B1-C17
A49-B1-C17
A50-B1-C17
A51-B1-C17
A52-B1-C17
A53-B1-C17
A54-B1-C17
A55-B1-C17
A56-B1-C17
A57-B1-C17
A58-B1-C17
A59-B1-C17
A60-B1-C17
A61-B1-C17
A62-B1-C17
A63-B1-C17
A64-B1-C17
A65-B1-C17
A66-B1-C17
A67-B1-C17
A68-B1-C17
A69-B1-C17
A70-B1-C17
A71-B1-C17
A72-B1-C17
A73-B1-C17
A74-B1-C17
A75-B1-C17
A76-B1-C17
A77-B1-C17
A1-B2-C17
A2-B2-C17
A3-B2-C17
A4-B2-C17
A5-B2-C17
A6-B2-C17
A7-B2-C17
A8-B2-C17
A9-B2-C17
A10-B2-C17
A11-B2-C17
A12-B2-C17
A13-B2-C17
A14-B2-C17
A15-B2-C17
A16-B2-C17
A17-B2-C17
A18-B2-C17
A19-B2-C17
A20-B2-C17
A21-B2-C17
A22-B2-C17
A23-B2-C17
A24-B2-C17
A25-B2-C17
A26-B2-C17
A27-B2-C17
A28-B2-C17
A29-B2-C17
A30-B2-C17
A31-B2-C17
A32-B2-C17
A33-B2-C17
A34-B2-C17
A35-B2-C17
A36-B2-C17
A37-B2-C17
A38-B2-C17
A39-B2-C17
A40-B2-C17
A41-B2-C17
A42-B2-C17
A43-B2-C17
A44-B2-C17
A45-B2-C17
A46-B2-C17
A47-B2-C17
A48-B2-C17
A49-B2-C17
A50-B2-C17
A51-B2-C17
A52-B2-C17
A53-B2-C17
A54-B2-C17
A55-B2-C17
A56-B2-C17
A57-B2-C17
A58-B2-C17
A59-B2-C17
A60-B2-C17
A61-B2-C17
A62-B2-C17
A63-B2-C17
A64-B2-C17
A65-B2-C17
A66-B2-C17
A67-B2-C17
A68-B2-C17
A69-B2-C17
A70-B2-C17
A71-B2-C17
A72-B2-C17
A73-B2-C17
A74-B2-C17
A75-B2-C17
A76-B2-C17
A77-B2-C17
A1-B3-C17
A2-B3-C17

A3-B3-C17
A4-B3-C17
A5-B3-C17
A6-B3-C17
A7-B3-C17
A8-B3-C17
A9-B3-C17
A10-B3-C17
A11-B3-C17
A12-B3-C17
A13-B3-C17
A14-B3-C17
A15-B3-C17
A16-B3-C17
A17-B3-C17
A18-B3-C17
A19-B3-C17
A20-B3-C17
A21-B3-C17
A22-B3-C17
A23-B3-C17
A24-B3-C17
A25-B3-C17
A26-B3-C17
A27-B3-C17
A28-B3-C17
A29-B3-C17
A30-B3-C17
A31-B3-C17
A32-B3-C17
A33-B3-C17
A34-B3-C17
A35-B3-C17
A36-B3-C17
A37-B3-C17
A38-B3-C17
A39-B3-C17
A40-B3-C17
A41-B3-C17
A42-B3-C17
A43-B3-C17
A44-B3-C17
A45-B3-C17
A46-B3-C17
A47-B3-C17
A48-B3-C17
A49-B3-C17
A50-B3-C17
A51-B3-C17
A52-B3-C17
A53-B3-C17
A54-B3-C17
A55-B3-C17
A56-B3-C17
A57-B3-C17
A58-B3-C17
A59-B3-C17
A60-B3-C17
A61-B3-C17
A62-B3-C17
A63-B3-C17
A64-B3-C17
A65-B3-C17
A66-B3-C17
A67-B3-C17
A68-B3-C17
A69-B3-C17
A70-B3-C17
A71-B3-C17
A72-B3-C17
A73-B3-C17
A74-B3-C17
A75-B3-C17
A76-B3-C17
A77-B3-C17
A1-B4-C17
A2-B4-C17
A3-B4-C17
A4-B4-C17
A5-B4-C17
A6-B4-C17
A7-B4-C17
A8-B4-C17
A9-B4-C17
A10-B4-C17
A11-B4-C17
A12-B4-C17
A13-B4-C17
A14-B4-C17
A15-B4-C17
A16-B4-C17
A17-B4-C17
A18-B4-C17
A19-B4-C17
A20-B4-C17
A21-B4-C17
A22-B4-C17
A23-B4-C17
A24-B4-C17
A25-B4-C17
A26-B4-C17
A27-B4-C17
A28-B4-C17
A29-B4-C17
A30-B4-C17
A31-B4-C17
A32-B4-C17
A33-B4-C17
A34-B4-C17
A35-B4-C17
A36-B4-C17
A37-B4-C17
A38-B4-C17
A39-B4-C17
A40-B4-C17
A41-B4-C17
A42-B4-C17
A43-B4-C17
A44-B4-C17
A45-B4-C17
A46-B4-C17
A47-B4-C17
A48-B4-C17
A49-B4-C17
A50-B4-C17
A51-B4-C17
A52-B4-C17
A53-B4-C17
A54-B4-C17
A55-B4-C17
A56-B4-C17
A57-B4-C17
A58-B4-C17
A59-B4-C17
A60-B4-C17
A61-B4-C17
A62-B4-C17
A63-B4-C17
A64-B4-C17
A65-B4-C17
A66-B4-C17
A67-B4-C17
A68-B4-C17
A69-B4-C17
A70-B4-C17
A71-B4-C17
A72-B4-C17
A73-B4-C17
A74-B4-C17
A75-B4-C17
A76-B4-C17
A77-B4-C17
A1-B1-C18
A2-B1-C18
A3-B1-C18
A4-B1-C18
A5-B1-C18
A6-B1-C18
A7-B1-C18
A8-B1-C18
A9-B1-C18
A10-B1-C18
A11-B1-C18
A12-B1-C18
A13-B1-C18
A14-B1-C18
A15-B1-C18
A16-B1-C18
A17-B1-C18
A18-B1-C18
A19-B1-C18
A20-B1-C18
A21-B1-C18
A22-B1-C18
A23-B1-C18
A24-B1-C18
A25-B1-C18
A26-B1-C18
A27-B1-C18
A28-B1-C18
A29-B1-C18
A30-B1-C18
A31-B1-C18
A32-B1-C18
A33-B1-C18
A34-B1-C18
A35-B1-C18
A36-B1-C18
A37-B1-C18
A38-B1-C18
A39-B1-C18
A40-B1-C18
A41-B1-C18
A42-B1-C18
A43-B1-C18
A44-B1-C18
A45-B1-C18
A46-B1-C18
A47-B1-C18
A48-B1-C18
A49-B1-C18
A50-B1-C18
A51-B1-C18
A52-B1-C18
A53-B1-C18
A54-B1-C18
A55-B1-C18
A56-B1-C18
A57-B1-C18
A58-B1-C18
A59-B1-C18
A60-B1-C18
A61-B1-C18
A62-B1-C18
A63-B1-C18
A64-B1-C18
A65-B1-C18
A66-B1-C18
A67-B1-C18
A68-B1-C18
A69-B1-C18
A70-B1-C18
A71-B1-C18
A72-B1-C18
A73-B1-C18
A74-B1-C18
A75-B1-C18
A76-B1-C18
A77-B1-C18
A1-B2-C18
A2-B2-C18
A3-B2-C18
A4-B2-C18
A5-B2-C18
A6-B2-C18
A7-B2-C18
A8-B2-C18
A9-B2-C18
A10-B2-C18
A11-B2-C18
A12-B2-C18
A13-B2-C18
A14-B2-C18
A15-B2-C18
A16-B2-C18
A17-B2-C18
A18-B2-C18
A19-B2-C18
A20-B2-C18
A21-B2-C18
A22-B2-C18
A23-B2-C18
A24-B2-C18
A25-B2-C18
A26-B2-C18
A27-B2-C18
A28-B2-C18
A29-B2-C18
A30-B2-C18
A31-B2-C18
A32-B2-C18
A33-B2-C18
A34-B2-C18
A35-B2-C18

A36-B2-C18
A37-B2-C18
A38-B2-C18
A39-B2-C18
A40-B2-C18
A41-B2-C18
A42-B2-C18
A43-B2-C18
A44-B2-C18
A45-B2-C18
A46-B2-C18
A47-B2-C18
A48-B2-C18
A49-B2-C18
A50-B2-C18
A51-B2-C18
A52-B2-C18
A53-B2-C18
A54-B2-C18
A55-B2-C18
A56-B2-C18
A57-B2-C18
A58-B2-C18
A59-B2-C18
A60-B2-C18
A61-B2-C18
A62-B2-C18
A63-B2-C18
A64-B2-C18
A65-B2-C18
A66-B2-C18
A67-B2-C18
A68-B2-C18
A69-B2-C18
A70-B2-C18
A71-B2-C18
A72-B2-C18
A73-B2-C18
A74-B2-C18
A75-B2-C18
A76-B2-C18
A77-B2-C18
A1-B3-C18
A2-B3-C18
A3-B3-C18
A4-B3-C18
A5-B3-C18
A6-B3-C18
A7-B3-C18
A8-B3-C18
A9-B3-C18
A10-B3-C18
A11-B3-C18
A12-B3-C18
A13-B3-C18
A14-B3-C18
A15-B3-C18
A16-B3-C18
A17-B3-C18
A18-B3-C18
A19-B3-C18
A20-B3-C18
A21-B3-C18
A22-B3-C18
A23-B3-C18
A24-B3-C18
A25-B3-C18
A26-B3-C18
A27-B3-C18
A28-B3-C18
A29-B3-C18
A30-B3-C18
A31-B3-C18
A32-B3-C18
A33-B3-C18
A34-B3-C18
A35-B3-C18
A36-B3-C18
A37-B3-C18
A38-B3-C18
A39-B3-C18
A40-B3-C18
A41-B3-C18
A42-B3-C18
A43-B3-C18
A44-B3-C18
A45-B3-C18
A46-B3-C18
A47-B3-C18
A48-B3-C18
A49-B3-C18
A50-B3-C18
A51-B3-C18
A52-B3-C18
A53-B3-C18
A54-B3-C18
A55-B3-C18
A56-B3-C18
A57-B3-C18
A58-B3-C18
A59-B3-C18
A60-B3-C18
A61-B3-C18
A62-B3-C18
A63-B3-C18
A64-B3-C18
A65-B3-C18
A66-B3-C18
A67-B3-C18
A68-B3-C18
A69-B3-C18
A70-B3-C18
A71-B3-C18
A72-B3-C18
A73-B3-C18
A74-B3-C18
A75-B3-C18
A76-B3-C18
A77-B3-C18
A1-B4-C18
A2-B4-C18
A3-B4-C18
A4-B4-C18
A5-B4-C18
A6-B4-C18
A7-B4-C18
A8-B4-C18
A9-B4-C18
A10-B4-C18
A11-B4-C18
A12-B4-C18
A13-B4-C18
A14-B4-C18
A15-B4-C18
A16-B4-C18
A17-B4-C18
A18-B4-C18
A19-B4-C18
A20-B4-C18
A21-B4-C18
A22-B4-C18
A23-B4-C18
A24-B4-C18
A25-B4-C18
A26-B4-C18
A27-B4-C18
A28-B4-C18
A29-B4-C18
A30-B4-C18
A31-B4-C18
A32-B4-C18
A33-B4-C18
A34-B4-C18
A35-B4-C18
A36-B4-C18
A37-B4-C18
A38-B4-C18
A39-B4-C18
A40-B4-C18
A41-B4-C18
A42-B4-C18
A43-B4-C18
A44-B4-C18
A45-B4-C18
A46-B4-C18
A47-B4-C18
A48-B4-C18
A49-B4-C18
A50-B4-C18
A51-B4-C18
A52-B4-C18
A53-B4-C18
A54-B4-C18
A55-B4-C18
A56-B4-C18
A57-B4-C18
A58-B4-C18
A59-B4-C18
A60-B4-C18
A61-B4-C18
A62-B4-C18
A63-B4-C18
A64-B4-C18
A65-B4-C18
A66-B4-C18
A67-B4-C18
A68-B4-C18
A69-B4-C18
A70-B4-C18
A71-B4-C18
A72-B4-C18
A73-B4-C18
A74-B4-C18
A75-B4-C18
A76-B4-C18
A77-B4-C18
A1-B1-C19
A2-B1-C19
A3-B1-C19
A4-B1-C19
A5-B1-C19
A6-B1-C19
A7-B1-C19
A8-B1-C19
A9-B1-C19
A10-B1-C19
A11-B1-C19
A12-B1-C19
A13-B1-C19
A14-B1-C19
A15-B1-C19
A16-B1-C19
A17-B1-C19
A18-B1-C19
A19-B1-C19
A20-B1-C19
A21-B1-C19
A22-B1-C19
A23-B1-C19
A24-B1-C19
A25-B1-C19
A26-B1-C19
A27-B1-C19
A28-B1-C19
A29-B1-C19
A30-B1-C19
A31-B1-C19
A32-B1-C19
A33-B1-C19
A34-B1-C19
A35-B1-C19
A36-B1-C19
A37-B1-C19
A38-B1-C19
A39-B1-C19
A40-B1-C19
A41-B1-C19
A42-B1-C19
A43-B1-C19
A44-B1-C19
A45-B1-C19
A46-B1-C19
A47-B1-C19
A48-B1-C19
A49-B1-C19
A50-B1-C19
A51-B1-C19
A52-B1-C19
A53-B1-C19
A54-B1-C19
A55-B1-C19
A56-B1-C19
A57-B1-C19
A58-B1-C19
A59-B1-C19
A60-B1-C19
A61-B1-C19
A62-B1-C19
A63-B1-C19
A64-B1-C19
A65-B1-C19
A66-B1-C19
A67-B1-C19
A68-B1-C19

A69-B1-C19
A70-B1-C19
A71-B1-C19
A72-B1-C19
A73-B1-C19
A74-B1-C19
A75-B1-C19
A76-B1-C19
A77-B1-C19
A1-B2-C19
A2-B2-C19
A3-B2-C19
A4-B2-C19
A5-B2-C19
A6-B2-C19
A7-B2-C19
A8-B2-C19
A9-B2-C19
A10-B2-C19
A11-B2-C19
A12-B2-C19
A13-B2-C19
A14-B2-C19
A15-B2-C19
A16-B2-C19
A17-B2-C19
A18-B2-C19
A19-B2-C19
A20-B2-C19
A21-B2-C19
A22-B2-C19
A23-B2-C19
A24-B2-C19
A25-B2-C19
A26-B2-C19
A27-B2-C19
A28-B2-C19
A29-B2-C19
A30-B2-C19
A31-B2-C19
A32-B2-C19
A33-B2-C19
A34-B2-C19
A35-B2-C19
A36-B2-C19
A37-B2-C19
A38-B2-C19
A39-B2-C19
A40-B2-C19
A41-B2-C19
A42-B2-C19
A43-B2-C19
A44-B2-C19
A45-B2-C19
A46-B2-C19
A47-B2-C19
A48-B2-C19
A49-B2-C19
A50-B2-C19
A51-B2-C19
A52-B2-C19
A53-B2-C19
A54-B2-C19
A55-B2-C19
A56-B2-C19
A57-B2-C19
A58-B2-C19
A59-B2-C19
A60-B2-C19
A61-B2-C19
A62-B2-C19
A63-B2-C19
A64-B2-C19
A65-B2-C19
A66-B2-C19
A67-B2-C19
A68-B2-C19
A69-B2-C19
A70-B2-C19
A71-B2-C19
A72-B2-C19
A73-B2-C19
A74-B2-C19
A75-B2-C19
A76-B2-C19
A77-B2-C19
A1-B3-C19
A2-B3-C19
A3-B3-C19
A4-B3-C19
A5-B3-C19
A6-B3-C19
A7-B3-C19
A8-B3-C19
A9-B3-C19
A10-B3-C19
A11-B3-C19
A12-B3-C19
A13-B3-C19
A14-B3-C19
A15-B3-C19
A16-B3-C19
A17-B3-C19
A18-B3-C19
A19-B3-C19
A20-B3-C19
A21-B3-C19
A22-B3-C19
A23-B3-C19
A24-B3-C19
A25-B3-C19
A26-B3-C19
A27-B3-C19
A28-B3-C19
A29-B3-C19
A30-B3-C19
A31-B3-C19
A32-B3-C19
A33-B3-C19
A34-B3-C19
A35-B3-C19
A36-B3-C19
A37-B3-C19
A38-B3-C19
A39-B3-C19
A40-B3-C19
A41-B3-C19
A42-B3-C19
A43-B3-C19
A44-B3-C19
A45-B3-C19
A46-B3-C19
A47-B3-C19
A48-B3-C19
A49-B3-C19
A50-B3-C19
A51-B3-C19
A52-B3-C19
A53-B3-C19
A54-B3-C19
A55-B3-C19
A56-B3-C19
A57-B3-C19
A58-B3-C19
A59-B3-C19
A60-B3-C19
A61-B3-C19
A62-B3-C19
A63-B3-C19
A64-B3-C19
A65-B3-C19
A66-B3-C19
A67-B3-C19
A68-B3-C19
A69-B3-C19
A70-B3-C19
A71-B3-C19
A72-B3-C19
A73-B3-C19
A74-B3-C19
A75-B3-C19
A76-B3-C19
A77-B3-C19
A1-B4-C19
A2-B4-C19
A3-B4-C19
A4-B4-C19
A5-B4-C19
A6-B4-C19
A7-B4-C19
A8-B4-C19
A9-B4-C19
A10-B4-C19
A11-B4-C19
A12-B4-C19
A13-B4-C19
A14-B4-C19
A15-B4-C19
A16-B4-C19
A17-B4-C19
A18-B4-C19
A19-B4-C19
A20-B4-C19
A21-B4-C19
A22-B4-C19
A23-B4-C19
A24-B4-C19
A25-B4-C19
A26-B4-C19
A27-B4-C19
A28-B4-C19
A29-B4-C19
A30-B4-C19
A31-B4-C19
A32-B4-C19
A33-B4-C19
A34-B4-C19
A35-B4-C19
A36-B4-C19
A37-B4-C19
A38-B4-C19
A39-B4-C19
A40-B4-C19
A41-B4-C19
A42-B4-C19
A43-B4-C19
A44-B4-C19
A45-B4-C19
A46-B4-C19
A47-B4-C19
A48-B4-C19
A49-B4-C19
A50-B4-C19
A51-B4-C19
A52-B4-C19
A53-B4-C19
A54-B4-C19
A55-B4-C19
A56-B4-C19
A57-B4-C19
A58-B4-C19
A59-B4-C19
A60-B4-C19
A61-B4-C19
A62-B4-C19
A63-B4-C19
A64-B4-C19
A65-B4-C19
A66-B4-C19
A67-B4-C19
A68-B4-C19
A69-B4-C19
A70-B4-C19
A71-B4-C19
A72-B4-C19
A73-B4-C19
A74-B4-C19
A75-B4-C19
A76-B4-C19
A77-B4-C19
A1-B1-C20
A2-B1-C20
A3-B1-C20
A4-B1-C20
A5-B1-C20
A6-B1-C20
A7-B1-C20
A8-B1-C20
A9-B1-C20
A10-B1-C20
A11-B1-C20
A12-B1-C20
A13-B1-C20
A14-B1-C20
A15-B1-C20
A16-B1-C20
A17-B1-C20
A18-B1-C20
A19-B1-C20
A20-B1-C20
A21-B1-C20
A22-B1-C20
A23-B1-C20
A24-B1-C20

A25-B1-C20
A26-B1-C20
A27-B1-C20
A28-B1-C20
A29-B1-C20
A30-B1-C20
A31-B1-C20
A32-B1-C20
A33-B1-C20
A34-B1-C20
A35-B1-C20
A36-B1-C20
A37-B1-C20
A38-B1-C20
A39-B1-C20
A40-B1-C20
A41-B1-C20
A42-B1-C20
A43-B1-C20
A44-B1-C20
A45-B1-C20
A46-B1-C20
A47-B1-C20
A48-B1-C20
A49-B1-C20
A50-B1-C20
A51-B1-C20
A52-B1-C20
A53-B1-C20
A54-B1-C20
A55-B1-C20
A56-B1-C20
A57-B1-C20
A58-B1-C20
A59-B1-C20
A60-B1-C20
A61-B1-C20
A62-B1-C20
A63-B1-C20
A64-B1-C20
A65-B1-C20
A66-B1-C20
A67-B1-C20
A68-B1-C20
A69-B1-C20
A70-B1-C20
A71-B1-C20
A72-B1-C20
A73-B1-C20
A74-B1-C20
A75-B1-C20
A76-B1-C20
A77-B1-C20
A1-B2-C20
A2-B2-C20
A3-B2-C20
A4-B2-C20
A5-B2-C20
A6-B2-C20
A7-B2-C20
A8-B2-C20
A9-B2-C20
A10-B2-C20
A11-B2-C20
A12-B2-C20
A13-B2-C20
A14-B2-C20
A15-B2-C20
A16-B2-C20
A17-B2-C20
A18-B2-C20
A19-B2-C20
A20-B2-C20
A21-B2-C20
A22-B2-C20
A23-B2-C20
A24-B2-C20
A25-B2-C20
A26-B2-C20
A27-B2-C20
A28-B2-C20
A29-B2-C20
A30-B2-C20
A31-B2-C20
A32-B2-C20
A33-B2-C20
A34-B2-C20
A35-B2-C20
A36-B2-C20
A37-B2-C20
A38-B2-C20
A39-B2-C20
A40-B2-C20
A41-B2-C20
A42-B2-C20
A43-B2-C20
A44-B2-C20
A45-B2-C20
A46-B2-C20
A47-B2-C20
A48-B2-C20
A49-B2-C20
A50-B2-C20
A51-B2-C20
A52-B2-C20
A53-B2-C20
A54-B2-C20
A55-B2-C20
A56-B2-C20
A57-B2-C20
A58-B2-C20
A59-B2-C20
A60-B2-C20
A61-B2-C20
A62-B2-C20
A63-B2-C20
A64-B2-C20
A65-B2-C20
A66-B2-C20
A67-B2-C20
A68-B2-C20
A69-B2-C20
A70-B2-C20
A71-B2-C20
A72-B2-C20
A73-B2-C20
A74-B2-C20
A75-B2-C20
A76-B2-C20
A77-B2-C20
A1-B3-C20
A2-B3-C20
A3-B3-C20
A4-B3-C20
A5-B3-C20
A6-B3-C20
A7-B3-C20
A8-B3-C20
A9-B3-C20
A10-B3-C20
A11-B3-C20
A12-B3-C20
A13-B3-C20
A14-B3-C20
A15-B3-C20
A16-B3-C20
A17-B3-C20
A18-B3-C20
A19-B3-C20
A20-B3-C20
A21-B3-C20
A22-B3-C20
A23-B3-C20
A24-B3-C20
A25-B3-C20
A26-B3-C20
A27-B3-C20
A28-B3-C20
A29-B3-C20
A30-B3-C20
A31-B3-C20
A32-B3-C20
A33-B3-C20
A34-B3-C20
A35-B3-C20
A36-B3-C20
A37-B3-C20
A38-B3-C20
A39-B3-C20
A40-B3-C20
A41-B3-C20
A42-B3-C20
A43-B3-C20
A44-B3-C20
A45-B3-C20
A46-B3-C20
A47-B3-C20
A48-B3-C20
A49-B3-C20
A50-B3-C20
A51-B3-C20
A52-B3-C20
A53-B3-C20
A54-B3-C20
A55-B3-C20
A56-B3-C20
A57-B3-C20
A58-B3-C20
A59-B3-C20
A60-B3-C20
A61-B3-C20
A62-B3-C20
A63-B3-C20
A64-B3-C20
A65-B3-C20
A66-B3-C20
A67-B3-C20
A68-B3-C20
A69-B3-C20
A70-B3-C20
A71-B3-C20
A72-B3-C20
A73-B3-C20
A74-B3-C20
A75-B3-C20
A76-B3-C20
A77-B3-C20
A1-B4-C20
A2-B4-C20
A3-B4-C20
A4-B4-C20
A5-B4-C20
A6-B4-C20
A7-B4-C20
A8-B4-C20
A9-B4-C20
A10-B4-C20
A11-B4-C20
A12-B4-C20
A13-B4-C20
A14-B4-C20
A15-B4-C20
A16-B4-C20
A17-B4-C20
A18-B4-C20
A19-B4-C20
A20-B4-C20
A21-B4-C20
A22-B4-C20
A23-B4-C20
A24-B4-C20
A25-B4-C20
A26-B4-C20
A27-B4-C20
A28-B4-C20
A29-B4-C20
A30-B4-C20
A31-B4-C20
A32-B4-C20
A33-B4-C20
A34-B4-C20
A35-B4-C20
A36-B4-C20
A37-B4-C20
A38-B4-C20
A39-B4-C20
A40-B4-C20
A41-B4-C20
A42-B4-C20
A43-B4-C20
A44-B4-C20
A45-B4-C20
A46-B4-C20
A47-B4-C20
A48-B4-C20
A49-B4-C20
A50-B4-C20
A51-B4-C20
A52-B4-C20
A53-B4-C20
A54-B4-C20
A55-B4-C20
A56-B4-C20
A57-B4-C20

A58-B4-C20
A59-B4-C20
A60-B4-C20
A61-B4-C20
A62-B4-C20
A63-B4-C20
A64-B4-C20
A65-B4-C20
A66-B4-C20
A67-B4-C20
A68-B4-C20
A69-B4-C20
A70-B4-C20
A71-B4-C20
A72-B4-C20
A73-B4-C20
A74-B4-C20
A75-B4-C20
A76-B4-C20
A77-B4-C20
A1-B1-C21
A2-B1-C21
A3-B1-C21
A4-B1-C21
A5-B1-C21
A6-B1-C21
A7-B1-C21
A8-B1-C21
A9-B1-C21
A10-B1-C21
A11-B1-C21
A12-B1-C21
A13-B1-C21
A14-B1-C21
A15-B1-C21
A16-B1-C21
A17-B1-C21
A18-B1-C21
A19-B1-C21
A20-B1-C21
A21-B1-C21
A22-B1-C21
A23-B1-C21
A24-B1-C21
A25-B1-C21
A26-B1-C21
A27-B1-C21
A28-B1-C21
A29-B1-C21
A30-B1-C21
A31-B1-C21
A32-B1-C21
A33-B1-C21
A34-B1-C21
A35-B1-C21
A36-B1-C21
A37-B1-C21
A38-B1-C21
A39-B1-C21
A40-B1-C21
A41-B1-C21
A42-B1-C21
A43-B1-C21
A44-B1-C21
A45-B1-C21
A46-B1-C21
A47-B1-C21
A48-B1-C21
A49-B1-C21
A50-B1-C21
A51-B1-C21
A52-B1-C21
A53-B1-C21
A54-B1-C21
A55-B1-C21
A56-B1-C21
A57-B1-C21
A58-B1-C21
A59-B1-C21
A60-B1-C21
A61-B1-C21
A62-B1-C21
A63-B1-C21
A64-B1-C21
A65-B1-C21
A66-B1-C21
A67-B1-C21
A68-B1-C21
A69-B1-C21
A70-B1-C21
A71-B1-C21
A72-B1-C21
A73-B1-C21
A74-B1-C21
A75-B1-C21
A76-B1-C21
A77-B1-C21
A1-B2-C21
A2-B2-C21
A3-B2-C21
A4-B2-C21
A5-B2-C21
A6-B2-C21
A7-B2-C21
A8-B2-C21
A9-B2-C21
A10-B2-C21
A11-B2-C21
A12-B2-C21
A13-B2-C21
A14-B2-C21
A15-B2-C21
A16-B2-C21
A17-B2-C21
A18-B2-C21
A19-B2-C21
A20-B2-C21
A21-B2-C21
A22-B2-C21
A23-B2-C21
A24-B2-C21
A25-B2-C21
A26-B2-C21
A27-B2-C21
A28-B2-C21
A29-B2-C21
A30-B2-C21
A31-B2-C21
A32-B2-C21
A33-B2-C21
A34-B2-C21
A35-B2-C21
A36-B2-C21
A37-B2-C21
A38-B2-C21
A39-B2-C21
A40-B2-C21
A41-B2-C21
A42-B2-C21
A43-B2-C21
A44-B2-C21
A45-B2-C21
A46-B2-C21
A47-B2-C21
A48-B2-C21
A49-B2-C21
A50-B2-C21
A51-B2-C21
A52-B2-C21
A53-B2-C21
A54-B2-C21
A55-B2-C21
A56-B2-C21
A57-B2-C21
A58-B2-C21
A59-B2-C21
A60-B2-C21
A61-B2-C21
A62-B2-C21
A63-B2-C21
A64-B2-C21
A65-B2-C21
A66-B2-C21
A67-B2-C21
A68-B2-C21
A69-B2-C21
A70-B2-C21
A71-B2-C21
A72-B2-C21
A73-B2-C21
A74-B2-C21
A75-B2-C21
A76-B2-C21
A77-B2-C21
A1-B3-C21
A2-B3-C21
A3-B3-C21
A4-B3-C21
A5-B3-C21
A6-B3-C21
A7-B3-C21
A8-B3-C21
A9-B3-C21
A10-B3-C21
A11-B3-C21
A12-B3-C21
A13-B3-C21
A14-B3-C21
A15-B3-C21
A16-B3-C21
A17-B3-C21
A18-B3-C21
A19-B3-C21
A20-B3-C21
A21-B3-C21
A22-B3-C21
A23-B3-C21
A24-B3-C21
A25-B3-C21
A26-B3-C21
A27-B3-C21
A28-B3-C21
A29-B3-C21
A30-B3-C21
A31-B3-C21
A32-B3-C21
A33-B3-C21
A34-B3-C21
A35-B3-C21
A36-B3-C21
A37-B3-C21
A38-B3-C21
A39-B3-C21
A40-B3-C21
A41-B3-C21
A42-B3-C21
A43-B3-C21
A44-B3-C21
A45-B3-C21
A46-B3-C21
A47-B3-C21
A48-B3-C21
A49-B3-C21
A50-B3-C21
A51-B3-C21
A52-B3-C21
A53-B3-C21
A54-B3-C21
A55-B3-C21
A56-B3-C21
A57-B3-C21
A58-B3-C21
A59-B3-C21
A60-B3-C21
A61-B3-C21
A62-B3-C21
A63-B3-C21
A64-B3-C21
A65-B3-C21
A66-B3-C21
A67-B3-C21
A68-B3-C21
A69-B3-C21
A70-B3-C21
A71-B3-C21
A72-B3-C21
A73-B3-C21
A74-B3-C21
A75-B3-C21
A76-B3-C21
A77-B3-C21
A1-B4-C21
A2-B4-C21
A3-B4-C21
A4-B4-C21
A5-B4-C21
A6-B4-C21
A7-B4-C21
A8-B4-C21
A9-B4-C21
A10-B4-C21
A11-B4-C21
A12-B4-C21
A13-B4-C21

A14-B4-C21
A15-B4-C21
A16-B4-C21
A17-B4-C21
A18-B4-C21
A19-B4-C21
A20-B4-C21
A21-B4-C21
A22-B4-C21
A23-B4-C21
A24-B4-C21
A25-B4-C21
A26-B4-C21
A27-B4-C21
A28-B4-C21
A29-B4-C21
A30-B4-C21
A31-B4-C21
A32-B4-C21
A33-B4-C21
A34-B4-C21
A35-B4-C21
A36-B4-C21
A37-B4-C21
A38-B4-C21
A39-B4-C21
A40-B4-C21
A41-B4-C21
A42-B4-C21
A43-B4-C21
A44-B4-C21
A45-B4-C21
A46-B4-C21
A47-B4-C21
A48-B4-C21
A49-B4-C21
A50-B4-C21
A51-B4-C21
A52-B4-C21
A53-B4-C21
A54-B4-C21
A55-B4-C21
A56-B4-C21
A57-B4-C21
A58-B4-C21
A59-B4-C21
A60-B4-C21
A61-B4-C21
A62-B4-C21
A63-B4-C21
A64-B4-C21
A65-B4-C21
A66-B4-C21
A67-B4-C21
A68-B4-C21
A69-B4-C21
A70-B4-C21
A71-B4-C21
A72-B4-C21
A73-B4-C21
A74-B4-C21
A75-B4-C21
A76-B4-C21
A77-B4-C21
A1-B1-C22
A2-B1-C22
A3-B1-C22
A4-B1-C22
A5-B1-C22
A6-B1-C22
A7-B1-C22
A8-B1-C22
A9-B1-C22
A10-B1-C22
A11-B1-C22
A12-B1-C22
A13-B1-C22
A14-B1-C22
A15-B1-C22
A16-B1-C22
A17-B1-C22
A18-B1-C22
A19-B1-C22
A20-B1-C22
A21-B1-C22
A22-B1-C22
A23-B1-C22
A24-B1-C22
A25-B1-C22
A26-B1-C22
A27-B1-C22
A28-B1-C22
A29-B1-C22
A30-B1-C22
A31-B1-C22
A32-B1-C22
A33-B1-C22
A34-B1-C22
A35-B1-C22
A36-B1-C22
A37-B1-C22
A38-B1-C22
A39-B1-C22
A40-B1-C22
A41-B1-C22
A42-B1-C22
A43-B1-C22
A44-B1-C22
A45-B1-C22
A46-B1-C22
A47-B1-C22
A48-B1-C22
A49-B1-C22
A50-B1-C22
A51-B1-C22
A52-B1-C22
A53-B1-C22
A54-B1-C22
A55-B1-C22
A56-B1-C22
A57-B1-C22
A58-B1-C22
A59-B1-C22
A60-B1-C22
A61-B1-C22
A62-B1-C22
A63-B1-C22
A64-B1-C22
A65-B1-C22
A66-B1-C22
A67-B1-C22
A68-B1-C22
A69-B1-C22
A70-B1-C22
A71-B1-C22
A72-B1-C22
A73-B1-C22
A74-B1-C22
A75-B1-C22
A76-B1-C22
A77-B1-C22
A1-B2-C22
A2-B2-C22
A3-B2-C22
A4-B2-C22
A5-B2-C22
A6-B2-C22
A7-B2-C22
A8-B2-C22
A9-B2-C22
A10-B2-C22
A11-B2-C22
A12-B2-C22
A13-B2-C22
A14-B2-C22
A15-B2-C22
A16-B2-C22
A17-B2-C22
A18-B2-C22
A19-B2-C22
A20-B2-C22
A21-B2-C22
A22-B2-C22
A23-B2-C22
A24-B2-C22
A25-B2-C22
A26-B2-C22
A27-B2-C22
A28-B2-C22
A29-B2-C22
A30-B2-C22
A31-B2-C22
A32-B2-C22
A33-B2-C22
A34-B2-C22
A35-B2-C22
A36-B2-C22
A37-B2-C22
A38-B2-C22
A39-B2-C22
A40-B2-C22
A41-B2-C22
A42-B2-C22
A43-B2-C22
A44-B2-C22
A45-B2-C22
A46-B2-C22
A47-B2-C22
A48-B2-C22
A49-B2-C22
A50-B2-C22
A51-B2-C22
A52-B2-C22
A53-B2-C22
A54-B2-C22
A55-B2-C22
A56-B2-C22
A57-B2-C22
A58-B2-C22
A59-B2-C22
A60-B2-C22
A61-B2-C22
A62-B2-C22
A63-B2-C22
A64-B2-C22
A65-B2-C22
A66-B2-C22
A67-B2-C22
A68-B2-C22
A69-B2-C22
A70-B2-C22
A71-B2-C22
A72-B2-C22
A73-B2-C22
A74-B2-C22
A75-B2-C22
A76-B2-C22
A77-B2-C22
A1-B3-C22
A2-B3-C22
A3-B3-C22
A4-B3-C22
A5-B3-C22
A6-B3-C22
A7-B3-C22
A8-B3-C22
A9-B3-C22
A10-B3-C22
A11-B3-C22
A12-B3-C22
A13-B3-C22
A14-B3-C22
A15-B3-C22
A16-B3-C22
A17-B3-C22
A18-B3-C22
A19-B3-C22
A20-B3-C22
A21-B3-C22
A22-B3-C22
A23-B3-C22
A24-B3-C22
A25-B3-C22
A26-B3-C22
A27-B3-C22
A28-B3-C22
A29-B3-C22
A30-B3-C22
A31-B3-C22
A32-B3-C22
A33-B3-C22
A34-B3-C22
A35-B3-C22
A36-B3-C22
A37-B3-C22
A38-B3-C22
A39-B3-C22
A40-B3-C22
A41-B3-C22
A42-B3-C22
A43-B3-C22
A44-B3-C22
A45-B3-C22
A46-B3-C22

A47-B3-C22
A48-B3-C22
A49-B3-C22
A50-B3-C22
A51-B3-C22
A52-B3-C22
A53-B3-C22
A54-B3-C22
A55-B3-C22
A56-B3-C22
A57-B3-C22
A58-B3-C22
A59-B3-C22
A60-B3-C22
A61-B3-C22
A62-B3-C22
A63-B3-C22
A64-B3-C22
A65-B3-C22
A66-B3-C22
A67-B3-C22
A68-B3-C22
A69-B3-C22
A70-B3-C22
A71-B3-C22
A72-B3-C22
A73-B3-C22
A74-B3-C22
A75-B3-C22
A76-B3-C22
A77-B3-C22
A1-B4-C22
A2-B4-C22
A3-B4-C22
A4-B4-C22
A5-B4-C22
A6-B4-C22
A7-B4-C22
A8-B4-C22
A9-B4-C22
A10-B4-C22
A11-B4-C22
A12-B4-C22
A13-B4-C22
A14-B4-C22
A15-B4-C22
A16-B4-C22
A17-B4-C22
A18-B4-C22
A19-B4-C22
A20-B4-C22
A21-B4-C22
A22-B4-C22
A23-B4-C22
A24-B4-C22
A25-B4-C22
A26-B4-C22
A27-B4-C22
A28-B4-C22
A29-B4-C22
A30-B4-C22
A31-B4-C22
A32-B4-C22
A33-B4-C22
A34-B4-C22
A35-B4-C22
A36-B4-C22
A37-B4-C22
A38-B4-C22
A39-B4-C22
A40-B4-C22
A41-B4-C22
A42-B4-C22
A43-B4-C22
A44-B4-C22
A45-B4-C22
A46-B4-C22
A47-B4-C22
A48-B4-C22
A49-B4-C22
A50-B4-C22
A51-B4-C22
A52-B4-C22
A53-B4-C22
A54-B4-C22
A55-B4-C22
A56-B4-C22
A57-B4-C22
A58-B4-C22
A59-B4-C22
A60-B4-C22
A61-B4-C22
A62-B4-C22
A63-B4-C22
A64-B4-C22
A65-B4-C22
A66-B4-C22
A67-B4-C22
A68-B4-C22
A69-B4-C22
A70-B4-C22
A71-B4-C22
A72-B4-C22
A73-B4-C22
A74-B4-C22
A75-B4-C22
A76-B4-C22
A77-B4-C22
A1-B1-C23
A2-B1-C23
A3-B1-C23
A4-B1-C23
A5-B1-C23
A6-B1-C23
A7-B1-C23
A8-B1-C23
A9-B1-C23
A10-B1-C23
A11-B1-C23
A12-B1-C23
A13-B1-C23
A14-B1-C23
A15-B1-C23
A16-B1-C23
A17-B1-C23
A18-B1-C23
A19-B1-C23
A20-B1-C23
A21-B1-C23
A22-B1-C23
A23-B1-C23
A24-B1-C23
A25-B1-C23
A26-B1-C23
A27-B1-C23
A28-B1-C23
A29-B1-C23
A30-B1-C23
A31-B1-C23
A32-B1-C23
A33-B1-C23
A34-B1-C23
A35-B1-C23
A36-B1-C23
A37-B1-C23
A38-B1-C23
A39-B1-C23
A40-B1-C23
A41-B1-C23
A42-B1-C23
A43-B1-C23
A44-B1-C23
A45-B1-C23
A46-B1-C23
A47-B1-C23
A48-B1-C23
A49-B1-C23
A50-B1-C23
A51-B1-C23
A52-B1-C23
A53-B1-C23
A54-B1-C23
A55-B1-C23
A56-B1-C23
A57-B1-C23
A58-B1-C23
A59-B1-C23
A60-B1-C23
A61-B1-C23
A62-B1-C23
A63-B1-C23
A64-B1-C23
A65-B1-C23
A66-B1-C23
A67-B1-C23
A68-B1-C23
A69-B1-C23
A70-B1-C23
A71-B1-C23
A72-B1-C23
A73-B1-C23
A74-B1-C23
A75-B1-C23
A76-B1-C23
A77-B1-C23
A1-B2-C23
A2-B2-C23
A3-B2-C23
A4-B2-C23
A5-B2-C23
A6-B2-C23
A7-B2-C23
A8-B2-C23
A9-B2-C23
A10-B2-C23
A11-B2-C23
A12-B2-C23
A13-B2-C23
A14-B2-C23
A15-B2-C23
A16-B2-C23
A17-B2-C23
A18-B2-C23
A19-B2-C23
A20-B2-C23
A21-B2-C23
A22-B2-C23
A23-B2-C23
A24-B2-C23
A25-B2-C23
A26-B2-C23
A27-B2-C23
A28-B2-C23
A29-B2-C23
A30-B2-C23
A31-B2-C23
A32-B2-C23
A33-B2-C23
A34-B2-C23
A35-B2-C23
A36-B2-C23
A37-B2-C23
A38-B2-C23
A39-B2-C23
A40-B2-C23
A41-B2-C23
A42-B2-C23
A43-B2-C23
A44-B2-C23
A45-B2-C23
A46-B2-C23
A47-B2-C23
A48-B2-C23
A49-B2-C23
A50-B2-C23
A51-B2-C23
A52-B2-C23
A53-B2-C23
A54-B2-C23
A55-B2-C23
A56-B2-C23
A57-B2-C23
A58-B2-C23
A59-B2-C23
A60-B2-C23
A61-B2-C23
A62-B2-C23
A63-B2-C23
A64-B2-C23
A65-B2-C23
A66-B2-C23
A67-B2-C23
A68-B2-C23
A69-B2-C23
A70-B2-C23
A71-B2-C23
A72-B2-C23
A73-B2-C23
A74-B2-C23
A75-B2-C23
A76-B2-C23
A77-B2-C23
A1-B3-C23
A2-B3-C23

A3-B3-C23
A4-B3-C23
A5-B3-C23
A6-B3-C23
A7-B3-C23
A8-B3-C23
A9-B3-C23
A10-B3-C23
A11-B3-C23
A12-B3-C23
A13-B3-C23
A14-B3-C23
A15-B3-C23
A16-B3-C23
A17-B3-C23
A18-B3-C23
A19-B3-C23
A20-B3-C23
A21-B3-C23
A22-B3-C23
A23-B3-C23
A24-B3-C23
A25-B3-C23
A26-B3-C23
A27-B3-C23
A28-B3-C23
A29-B3-C23
A30-B3-C23
A31-B3-C23
A32-B3-C23
A33-B3-C23
A34-B3-C23
A35-B3-C23
A36-B3-C23
A37-B3-C23
A38-B3-C23
A39-B3-C23
A40-B3-C23
A41-B3-C23
A42-B3-C23
A43-B3-C23
A44-B3-C23
A45-B3-C23
A46-B3-C23
A47-B3-C23
A48-B3-C23
A49-B3-C23
A50-B3-C23
A51-B3-C23
A52-B3-C23
A53-B3-C23
A54-B3-C23
A55-B3-C23
A56-B3-C23
A57-B3-C23
A58-B3-C23
A59-B3-C23
A60-B3-C23
A61-B3-C23
A62-B3-C23
A63-B3-C23
A64-B3-C23
A65-B3-C23
A66-B3-C23
A67-B3-C23
A68-B3-C23
A69-B3-C23
A70-B3-C23
A71-B3-C23
A72-B3-C23
A73-B3-C23
A74-B3-C23
A75-B3-C23
A76-B3-C23
A77-B3-C23
A1-B4-C23
A2-B4-C23
A3-B4-C23
A4-B4-C23
A5-B4-C23
A6-B4-C23
A7-B4-C23
A8-B4-C23
A9-B4-C23
A10-B4-C23
A11-B4-C23
A12-B4-C23
A13-B4-C23
A14-B4-C23
A15-B4-C23
A16-B4-C23
A17-B4-C23
A18-B4-C23
A19-B4-C23
A20-B4-C23
A21-B4-C23
A22-B4-C23
A23-B4-C23
A24-B4-C23
A25-B4-C23
A26-B4-C23
A27-B4-C23
A28-B4-C23
A29-B4-C23
A30-B4-C23
A31-B4-C23
A32-B4-C23
A33-B4-C23
A34-B4-C23
A35-B4-C23
A36-B4-C23
A37-B4-C23
A38-B4-C23
A39-B4-C23
A40-B4-C23
A41-B4-C23
A42-B4-C23
A43-B4-C23
A44-B4-C23
A45-B4-C23
A46-B4-C23
A47-B4-C23
A48-B4-C23
A49-B4-C23
A50-B4-C23
A51-B4-C23
A52-B4-C23
A53-B4-C23
A54-B4-C23
A55-B4-C23
A56-B4-C23
A57-B4-C23
A58-B4-C23
A59-B4-C23
A60-B4-C23
A61-B4-C23
A62-B4-C23
A63-B4-C23
A64-B4-C23
A65-B4-C23
A66-B4-C23
A67-B4-C23
A68-B4-C23
A69-B4-C23
A70-B4-C23
A71-B4-C23
A72-B4-C23
A73-B4-C23
A74-B4-C23
A75-B4-C23
A76-B4-C23
A77-B4-C23
A1-B1-C24
A2-B1-C24
A3-B1-C24
A4-B1-C24
A5-B1-C24
A6-B1-C24
A7-B1-C24
A8-B1-C24
A9-B1-C24
A10-B1-C24
A11-B1-C24
A12-B1-C24
A13-B1-C24
A14-B1-C24
A15-B1-C24
A16-B1-C24
A17-B1-C24
A18-B1-C24
A19-B1-C24
A20-B1-C24
A21-B1-C24
A22-B1-C24
A23-B1-C24
A24-B1-C24
A25-B1-C24
A26-B1-C24
A27-B1-C24
A28-B1-C24
A29-B1-C24
A30-B1-C24
A31-B1-C24
A32-B1-C24
A33-B1-C24
A34-B1-C24
A35-B1-C24
A36-B1-C24
A37-B1-C24
A38-B1-C24
A39-B1-C24
A40-B1-C24
A41-B1-C24
A42-B1-C24
A43-B1-C24
A44-B1-C24
A45-B1-C24
A46-B1-C24
A47-B1-C24
A48-B1-C24
A49-B1-C24
A50-B1-C24
A51-B1-C24
A52-B1-C24
A53-B1-C24
A54-B1-C24
A55-B1-C24
A56-B1-C24
A57-B1-C24
A58-B1-C24
A59-B1-C24
A60-B1-C24
A61-B1-C24
A62-B1-C24
A63-B1-C24
A64-B1-C24
A65-B1-C24
A66-B1-C24
A67-B1-C24
A68-B1-C24
A69-B1-C24
A70-B1-C24
A71-B1-C24
A72-B1-C24
A73-B1-C24
A74-B1-C24
A75-B1-C24
A76-B1-C24
A77-B1-C24
A1-B2-C24
A2-B2-C24
A3-B2-C24
A4-B2-C24
A5-B2-C24
A6-B2-C24
A7-B2-C24
A8-B2-C24
A9-B2-C24
A10-B2-C24
A11-B2-C24
A12-B2-C24
A13-B2-C24
A14-B2-C24
A15-B2-C24
A16-B2-C24
A17-B2-C24
A18-B2-C24
A19-B2-C24
A20-B2-C24
A21-B2-C24
A22-B2-C24
A23-B2-C24
A24-B2-C24
A25-B2-C24
A26-B2-C24
A27-B2-C24
A28-B2-C24
A29-B2-C24
A30-B2-C24
A31-B2-C24
A32-B2-C24
A33-B2-C24
A34-B2-C24
A35-B2-C24

A36-B2-C24
A37-B2-C24
A38-B2-C24
A39-B2-C24
A40-B2-C24
A41-B2-C24
A42-B2-C24
A43-B2-C24
A44-B2-C24
A45-B2-C24
A46-B2-C24
A47-B2-C24
A48-B2-C24
A49-B2-C24
A50-B2-C24
A51-B2-C24
A52-B2-C24
A53-B2-C24
A54-B2-C24
A55-B2-C24
A56-B2-C24
A57-B2-C24
A58-B2-C24
A59-B2-C24
A60-B2-C24
A61-B2-C24
A62-B2-C24
A63-B2-C24
A64-B2-C24
A65-B2-C24
A66-B2-C24
A67-B2-C24
A68-B2-C24
A69-B2-C24
A70-B2-C24
A71-B2-C24
A72-B2-C24
A73-B2-C24
A74-B2-C24
A75-B2-C24
A76-B2-C24
A77-B2-C24
A1-B3-C24
A2-B3-C24
A3-B3-C24
A4-B3-C24
A5-B3-C24
A6-B3-C24
A7-B3-C24
A8-B3-C24
A9-B3-C24
A10-B3-C24
A11-B3-C24
A12-B3-C24
A13-B3-C24
A14-B3-C24
A15-B3-C24
A16-B3-C24
A17-B3-C24
A18-B3-C24
A19-B3-C24
A20-B3-C24
A21-B3-C24
A22-B3-C24
A23-B3-C24
A24-B3-C24
A25-B3-C24
A26-B3-C24
A27-B3-C24
A28-B3-C24
A29-B3-C24
A30-B3-C24
A31-B3-C24
A32-B3-C24
A33-B3-C24
A34-B3-C24
A35-B3-C24
A36-B3-C24
A37-B3-C24
A38-B3-C24
A39-B3-C24
A40-B3-C24
A41-B3-C24
A42-B3-C24
A43-B3-C24
A44-B3-C24
A45-B3-C24
A46-B3-C24
A47-B3-C24
A48-B3-C24
A49-B3-C24
A50-B3-C24
A51-B3-C24
A52-B3-C24
A53-B3-C24
A54-B3-C24
A55-B3-C24
A56-B3-C24
A57-B3-C24
A58-B3-C24
A59-B3-C24
A60-B3-C24
A61-B3-C24
A62-B3-C24
A63-B3-C24
A64-B3-C24
A65-B3-C24
A66-B3-C24
A67-B3-C24
A68-B3-C24
A69-B3-C24
A70-B3-C24
A71-B3-C24
A72-B3-C24
A73-B3-C24
A74-B3-C24
A75-B3-C24
A76-B3-C24
A77-B3-C24
A1-B4-C24
A2-B4-C24
A3-B4-C24
A4-B4-C24
A5-B4-C24
A6-B4-C24
A7-B4-C24
A8-B4-C24
A9-B4-C24
A10-B4-C24
A11-B4-C24
A12-B4-C24
A13-B4-C24
A14-B4-C24
A15-B4-C24
A16-B4-C24
A17-B4-C24
A18-B4-C24
A19-B4-C24
A20-B4-C24
A21-B4-C24
A22-B4-C24
A23-B4-C24
A24-B4-C24
A25-B4-C24
A26-B4-C24
A27-B4-C24
A28-B4-C24
A29-B4-C24
A30-B4-C24
A31-B4-C24
A32-B4-C24
A33-B4-C24
A34-B4-C24
A35-B4-C24
A36-B4-C24
A37-B4-C24
A38-B4-C24
A39-B4-C24
A40-B4-C24
A41-B4-C24
A42-B4-C24
A43-B4-C24
A44-B4-C24
A45-B4-C24
A46-B4-C24
A47-B4-C24
A48-B4-C24
A49-B4-C24
A50-B4-C24
A51-B4-C24
A52-B4-C24
A53-B4-C24
A54-B4-C24
A55-B4-C24
A56-B4-C24
A57-B4-C24
A58-B4-C24
A59-B4-C24
A60-B4-C24
A61-B4-C24
A62-B4-C24
A63-B4-C24
A64-B4-C24
A65-B4-C24
A66-B4-C24
A67-B4-C24
A68-B4-C24
A69-B4-C24
A70-B4-C24
A71-B4-C24
A72-B4-C24
A73-B4-C24
A74-B4-C24
A75-B4-C24
A76-B4-C24
A77-B4-C24
A1-B1-C25
A2-B1-C25
A3-B1-C25
A4-B1-C25
A5-B1-C25
A6-B1-C25
A7-B1-C25
A8-B1-C25
A9-B1-C25
A10-B1-C25
A11-B1-C25
A12-B1-C25
A13-B1-C25
A14-B1-C25
A15-B1-C25
A16-B1-C25
A17-B1-C25
A18-B1-C25
A19-B1-C25
A20-B1-C25
A21-B1-C25
A22-B1-C25
A23-B1-C25
A24-B1-C25
A25-B1-C25
A26-B1-C25
A27-B1-C25
A28-B1-C25
A29-B1-C25
A30-B1-C25
A31-B1-C25
A32-B1-C25
A33-B1-C25
A34-B1-C25
A35-B1-C25
A36-B1-C25
A37-B1-C25
A38-B1-C25
A39-B1-C25
A40-B1-C25
A41-B1-C25
A42-B1-C25
A43-B1-C25
A44-B1-C25
A45-B1-C25
A46-B1-C25
A47-B1-C25
A48-B1-C25
A49-B1-C25
A50-B1-C25
A51-B1-C25
A52-B1-C25
A53-B1-C25
A54-B1-C25
A55-B1-C25
A56-B1-C25
A57-B1-C25
A58-B1-C25
A59-B1-C25
A60-B1-C25
A61-B1-C25
A62-B1-C25
A63-B1-C25
A64-B1-C25
A65-B1-C25
A66-B1-C25
A67-B1-C25
A68-B1-C25

A69-B1-C25
A70-B1-C25
A71-B1-C25
A72-B1-C25
A73-B1-C25
A74-B1-C25
A75-B1-C25
A76-B1-C25
A77-B1-C25
A1-B2-C25
A2-B2-C25
A3-B2-C25
A4-B2-C25
A5-B2-C25
A6-B2-C25
A7-B2-C25
A8-B2-C25
A9-B2-C25
A10-B2-C25
A11-B2-C25
A12-B2-C25
A13-B2-C25
A14-B2-C25
A15-B2-C25
A16-B2-C25
A17-B2-C25
A18-B2-C25
A19-B2-C25
A20-B2-C25
A21-B2-C25
A22-B2-C25
A23-B2-C25
A24-B2-C25
A25-B2-C25
A26-B2-C25
A27-B2-C25
A28-B2-C25
A29-B2-C25
A30-B2-C25
A31-B2-C25
A32-B2-C25
A33-B2-C25
A34-B2-C25
A35-B2-C25
A36-B2-C25
A37-B2-C25
A38-B2-C25
A39-B2-C25
A40-B2-C25
A41-B2-C25
A42-B2-C25
A43-B2-C25
A44-B2-C25
A45-B2-C25
A46-B2-C25
A47-B2-C25
A48-B2-C25
A49-B2-C25
A50-B2-C25
A51-B2-C25
A52-B2-C25
A53-B2-C25
A54-B2-C25
A55-B2-C25
A56-B2-C25
A57-B2-C25
A58-B2-C25
A59-B2-C25
A60-B2-C25
A61-B2-C25
A62-B2-C25
A63-B2-C25
A64-B2-C25
A65-B2-C25
A66-B2-C25
A67-B2-C25
A68-B2-C25
A69-B2-C25
A70-B2-C25
A71-B2-C25
A72-B2-C25
A73-B2-C25
A74-B2-C25
A75-B2-C25
A76-B2-C25
A77-B2-C25
A1-B3-C25
A2-B3-C25
A3-B3-C25
A4-B3-C25
A5-B3-C25
A6-B3-C25
A7-B3-C25
A8-B3-C25
A9-B3-C25
A10-B3-C25
A11-B3-C25
A12-B3-C25
A13-B3-C25
A14-B3-C25
A15-B3-C25
A16-B3-C25
A17-B3-C25
A18-B3-C25
A19-B3-C25
A20-B3-C25
A21-B3-C25
A22-B3-C25
A23-B3-C25
A24-B3-C25
A25-B3-C25
A26-B3-C25
A27-B3-C25
A28-B3-C25
A29-B3-C25
A30-B3-C25
A31-B3-C25
A32-B3-C25
A33-B3-C25
A34-B3-C25
A35-B3-C25
A36-B3-C25
A37-B3-C25
A38-B3-C25
A39-B3-C25
A40-B3-C25
A41-B3-C25
A42-B3-C25
A43-B3-C25
A44-B3-C25
A45-B3-C25
A46-B3-C25
A47-B3-C25
A48-B3-C25
A49-B3-C25
A50-B3-C25
A51-B3-C25
A52-B3-C25
A53-B3-C25
A54-B3-C25
A55-B3-C25
A56-B3-C25
A57-B3-C25
A58-B3-C25
A59-B3-C25
A60-B3-C25
A61-B3-C25
A62-B3-C25
A63-B3-C25
A64-B3-C25
A65-B3-C25
A66-B3-C25
A67-B3-C25
A68-B3-C25
A69-B3-C25
A70-B3-C25
A71-B3-C25
A72-B3-C25
A73-B3-C25
A74-B3-C25
A75-B3-C25
A76-B3-C25
A77-B3-C25
A1-B4-C25
A2-B4-C25
A3-B4-C25
A4-B4-C25
A5-B4-C25
A6-B4-C25
A7-B4-C25
A8-B4-C25
A9-B4-C25
A10-B4-C25
A11-B4-C25
A12-B4-C25
A13-B4-C25
A14-B4-C25
A15-B4-C25
A16-B4-C25
A17-B4-C25
A18-B4-C25
A19-B4-C25
A20-B4-C25
A21-B4-C25
A22-B4-C25
A23-B4-C25
A24-B4-C25
A25-B4-C25
A26-B4-C25
A27-B4-C25
A28-B4-C25
A29-B4-C25
A30-B4-C25
A31-B4-C25
A32-B4-C25
A33-B4-C25
A34-B4-C25
A35-B4-C25
A36-B4-C25
A37-B4-C25
A38-B4-C25
A39-B4-C25
A40-B4-C25
A41-B4-C25
A42-B4-C25
A43-B4-C25
A44-B4-C25
A45-B4-C25
A46-B4-C25
A47-B4-C25
A48-B4-C25
A49-B4-C25
A50-B4-C25
A51-B4-C25
A52-B4-C25
A53-B4-C25
A54-B4-C25
A55-B4-C25
A56-B4-C25
A57-B4-C25
A58-B4-C25
A59-B4-C25
A60-B4-C25
A61-B4-C25
A62-B4-C25
A63-B4-C25
A64-B4-C25
A65-B4-C25
A66-B4-C25
A67-B4-C25
A68-B4-C25
A69-B4-C25
A70-B4-C25
A71-B4-C25
A72-B4-C25
A73-B4-C25
A74-B4-C25
A75-B4-C25
A76-B4-C25
A77-B4-C25
A1-B1-C26
A2-B1-C26
A3-B1-C26
A4-B1-C26
A5-B1-C26
A6-B1-C26
A7-B1-C26
A8-B1-C26
A9-B1-C26
A10-B1-C26
A11-B1-C26
A12-B1-C26
A13-B1-C26
A14-B1-C26
A15-B1-C26
A16-B1-C26
A17-B1-C26
A18-B1-C26
A19-B1-C26
A20-B1-C26
A21-B1-C26
A22-B1-C26
A23-B1-C26
A24-B1-C26

A25-B1-C26
A26-B1-C26
A27-B1-C26
A28-B1-C26
A29-B1-C26
A30-B1-C26
A31-B1-C26
A32-B1-C26
A33-B1-C26
A34-B1-C26
A35-B1-C26
A36-B1-C26
A37-B1-C26
A38-B1-C26
A39-B1-C26
A40-B1-C26
A41-B1-C26
A42-B1-C26
A43-B1-C26
A44-B1-C26
A45-B1-C26
A46-B1-C26
A47-B1-C26
A48-B1-C26
A49-B1-C26
A50-B1-C26
A51-B1-C26
A52-B1-C26
A53-B1-C26
A54-B1-C26
A55-B1-C26
A56-B1-C26
A57-B1-C26
A58-B1-C26
A59-B1-C26
A60-B1-C26
A61-B1-C26
A62-B1-C26
A63-B1-C26
A64-B1-C26
A65-B1-C26
A66-B1-C26
A67-B1-C26
A68-B1-C26
A69-B1-C26
A70-B1-C26
A71-B1-C26
A72-B1-C26
A73-B1-C26
A74-B1-C26
A75-B1-C26
A76-B1-C26
A77-B1-C26
A1-B2-C26
A2-B2-C26
A3-B2-C26
A4-B2-C26
A5-B2-C26
A6-B2-C26
A7-B2-C26
A8-B2-C26
A9-B2-C26
A10-B2-C26
A11-B2-C26
A12-B2-C26
A13-B2-C26
A14-B2-C26
A15-B2-C26
A16-B2-C26
A17-B2-C26
A18-B2-C26
A19-B2-C26
A20-B2-C26
A21-B2-C26
A22-B2-C26
A23-B2-C26
A24-B2-C26
A25-B2-C26
A26-B2-C26
A27-B2-C26
A28-B2-C26
A29-B2-C26
A30-B2-C26
A31-B2-C26
A32-B2-C26
A33-B2-C26
A34-B2-C26
A35-B2-C26
A36-B2-C26
A37-B2-C26
A38-B2-C26
A39-B2-C26
A40-B2-C26
A41-B2-C26
A42-B2-C26
A43-B2-C26
A44-B2-C26
A45-B2-C26
A46-B2-C26
A47-B2-C26
A48-B2-C26
A49-B2-C26
A50-B2-C26
A51-B2-C26
A52-B2-C26
A53-B2-C26
A54-B2-C26
A55-B2-C26
A56-B2-C26
A57-B2-C26
A58-B2-C26
A59-B2-C26
A60-B2-C26
A61-B2-C26
A62-B2-C26
A63-B2-C26
A64-B2-C26
A65-B2-C26
A66-B2-C26
A67-B2-C26
A68-B2-C26
A69-B2-C26
A70-B2-C26
A71-B2-C26
A72-B2-C26
A73-B2-C26
A74-B2-C26
A75-B2-C26
A76-B2-C26
A77-B2-C26
A1-B3-C26
A2-B3-C26
A3-B3-C26
A4-B3-C26
A5-B3-C26
A6-B3-C26
A7-B3-C26
A8-B3-C26
A9-B3-C26
A10-B3-C26
A11-B3-C26
A12-B3-C26
A13-B3-C26
A14-B3-C26
A15-B3-C26
A16-B3-C26
A17-B3-C26
A18-B3-C26
A19-B3-C26
A20-B3-C26
A21-B3-C26
A22-B3-C26
A23-B3-C26
A24-B3-C26
A25-B3-C26
A26-B3-C26
A27-B3-C26
A28-B3-C26
A29-B3-C26
A30-B3-C26
A31-B3-C26
A32-B3-C26
A33-B3-C26
A34-B3-C26
A35-B3-C26
A36-B3-C26
A37-B3-C26
A38-B3-C26
A39-B3-C26
A40-B3-C26
A41-B3-C26
A42-B3-C26
A43-B3-C26
A44-B3-C26
A45-B3-C26
A46-B3-C26
A47-B3-C26
A48-B3-C26
A49-B3-C26
A50-B3-C26
A51-B3-C26
A52-B3-C26
A53-B3-C26
A54-B3-C26
A55-B3-C26
A56-B3-C26
A57-B3-C26
A58-B3-C26
A59-B3-C26
A60-B3-C26
A61-B3-C26
A62-B3-C26
A63-B3-C26
A64-B3-C26
A65-B3-C26
A66-B3-C26
A67-B3-C26
A68-B3-C26
A69-B3-C26
A70-B3-C26
A71-B3-C26
A72-B3-C26
A73-B3-C26
A74-B3-C26
A75-B3-C26
A76-B3-C26
A77-B3-C26
A1-B4-C26
A2-B4-C26
A3-B4-C26
A4-B4-C26
A5-B4-C26
A6-B4-C26
A7-B4-C26
A8-B4-C26
A9-B4-C26
A10-B4-C26
A11-B4-C26
A12-B4-C26
A13-B4-C26
A14-B4-C26
A15-B4-C26
A16-B4-C26
A17-B4-C26
A18-B4-C26
A19-B4-C26
A20-B4-C26
A21-B4-C26
A22-B4-C26
A23-B4-C26
A24-B4-C26
A25-B4-C26
A26-B4-C26
A27-B4-C26
A28-B4-C26
A29-B4-C26
A30-B4-C26
A31-B4-C26
A32-B4-C26
A33-B4-C26
A34-B4-C26
A35-B4-C26
A36-B4-C26
A37-B4-C26
A38-B4-C26
A39-B4-C26
A40-B4-C26
A41-B4-C26
A42-B4-C26
A43-B4-C26
A44-B4-C26
A45-B4-C26
A46-B4-C26
A47-B4-C26
A48-B4-C26
A49-B4-C26
A50-B4-C26
A51-B4-C26
A52-B4-C26
A53-B4-C26
A54-B4-C26
A55-B4-C26
A56-B4-C26
A57-B4-C26

A58-B4-C26
A59-B4-C26
A60-B4-C26
A61-B4-C26
A62-B4-C26
A63-B4-C26
A64-B4-C26
A65-B4-C26
A66-B4-C26
A67-B4-C26
A68-B4-C26
A69-B4-C26
A70-B4-C26
A71-B4-C26
A72-B4-C26
A73-B4-C26
A74-B4-C26
A75-B4-C26
A76-B4-C26
A77-B4-C26
A1-B1-C27
A2-B1-C27
A3-B1-C27
A4-B1-C27
A5-B1-C27
A6-B1-C27
A7-B1-C27
A8-B1-C27
A9-B1-C27
A10-B1-C27
A11-B1-C27
A12-B1-C27
A13-B1-C27
A14-B1-C27
A15-B1-C27
A16-B1-C27
A17-B1-C27
A18-B1-C27
A19-B1-C27
A20-B1-C27
A21-B1-C27
A22-B1-C27
A23-B1-C27
A24-B1-C27
A25-B1-C27
A26-B1-C27
A27-B1-C27
A28-B1-C27
A29-B1-C27
A30-B1-C27
A31-B1-C27
A32-B1-C27
A33-B1-C27
A34-B1-C27
A35-B1-C27
A36-B1-C27
A37-B1-C27
A38-B1-C27
A39-B1-C27
A40-B1-C27
A41-B1-C27
A42-B1-C27
A43-B1-C27
A44-B1-C27
A45-B1-C27
A46-B1-C27
A47-B1-C27
A48-B1-C27
A49-B1-C27
A50-B1-C27
A51-B1-C27
A52-B1-C27
A53-B1-C27
A54-B1-C27
A55-B1-C27
A56-B1-C27
A57-B1-C27
A58-B1-C27
A59-B1-C27
A60-B1-C27
A61-B1-C27
A62-B1-C27
A63-B1-C27
A64-B1-C27
A65-B1-C27
A66-B1-C27
A67-B1-C27
A68-B1-C27
A69-B1-C27
A70-B1-C27
A71-B1-C27
A72-B1-C27
A73-B1-C27
A74-B1-C27
A75-B1-C27
A76-B1-C27
A77-B1-C27
A1-B2-C27
A2-B2-C27
A3-B2-C27
A4-B2-C27
A5-B2-C27
A6-B2-C27
A7-B2-C27
A8-B2-C27
A9-B2-C27
A10-B2-C27
A11-B2-C27
A12-B2-C27
A13-B2-C27
A14-B2-C27
A15-B2-C27
A16-B2-C27
A17-B2-C27
A18-B2-C27
A19-B2-C27
A20-B2-C27
A21-B2-C27
A22-B2-C27
A23-B2-C27
A24-B2-C27
A25-B2-C27
A26-B2-C27
A27-B2-C27
A28-B2-C27
A29-B2-C27
A30-B2-C27
A31-B2-C27
A32-B2-C27
A33-B2-C27
A34-B2-C27
A35-B2-C27
A36-B2-C27
A37-B2-C27
A38-B2-C27
A39-B2-C27
A40-B2-C27
A41-B2-C27
A42-B2-C27
A43-B2-C27
A44-B2-C27
A45-B2-C27
A46-B2-C27
A47-B2-C27
A48-B2-C27
A49-B2-C27
A50-B2-C27
A51-B2-C27
A52-B2-C27
A53-B2-C27
A54-B2-C27
A55-B2-C27
A56-B2-C27
A57-B2-C27
A58-B2-C27
A59-B2-C27
A60-B2-C27
A61-B2-C27
A62-B2-C27
A63-B2-C27
A64-B2-C27
A65-B2-C27
A66-B2-C27
A67-B2-C27
A68-B2-C27
A69-B2-C27
A70-B2-C27
A71-B2-C27
A72-B2-C27
A73-B2-C27
A74-B2-C27
A75-B2-C27
A76-B2-C27
A77-B2-C27
A1-B3-C27
A2-B3-C27
A3-B3-C27
A4-B3-C27
A5-B3-C27
A6-B3-C27
A7-B3-C27
A8-B3-C27
A9-B3-C27
A10-B3-C27
A11-B3-C27
A12-B3-C27
A13-B3-C27
A14-B3-C27
A15-B3-C27
A16-B3-C27
A17-B3-C27
A18-B3-C27
A19-B3-C27
A20-B3-C27
A21-B3-C27
A22-B3-C27
A23-B3-C27
A24-B3-C27
A25-B3-C27
A26-B3-C27
A27-B3-C27
A28-B3-C27
A29-B3-C27
A30-B3-C27
A31-B3-C27
A32-B3-C27
A33-B3-C27
A34-B3-C27
A35-B3-C27
A36-B3-C27
A37-B3-C27
A38-B3-C27
A39-B3-C27
A40-B3-C27
A41-B3-C27
A42-B3-C27
A43-B3-C27
A44-B3-C27
A45-B3-C27
A46-B3-C27
A47-B3-C27
A48-B3-C27
A49-B3-C27
A50-B3-C27
A51-B3-C27
A52-B3-C27
A53-B3-C27
A54-B3-C27
A55-B3-C27
A56-B3-C27
A57-B3-C27
A58-B3-C27
A59-B3-C27
A60-B3-C27
A61-B3-C27
A62-B3-C27
A63-B3-C27
A64-B3-C27
A65-B3-C27
A66-B3-C27
A67-B3-C27
A68-B3-C27
A69-B3-C27
A70-B3-C27
A71-B3-C27
A72-B3-C27
A73-B3-C27
A74-B3-C27
A75-B3-C27
A76-B3-C27
A77-B3-C27
A1-B4-C27
A2-B4-C27
A3-B4-C27
A4-B4-C27
A5-B4-C27
A6-B4-C27
A7-B4-C27
A8-B4-C27
A9-B4-C27
A10-B4-C27
A11-B4-C27
A12-B4-C27
A13-B4-C27

A14-B4-C27
A15-B4-C27
A16-B4-C27
A17-B4-C27
A18-B4-C27
A19-B4-C27
A20-B4-C27
A21-B4-C27
A22-B4-C27
A23-B4-C27
A24-B4-C27
A25-B4-C27
A26-B4-C27
A27-B4-C27
A28-B4-C27
A29-B4-C27
A30-B4-C27
A31-B4-C27
A32-B4-C27
A33-B4-C27
A34-B4-C27
A35-B4-C27
A36-B4-C27
A37-B4-C27
A38-B4-C27
A39-B4-C27
A40-B4-C27
A41-B4-C27
A42-B4-C27
A43-B4-C27
A44-B4-C27
A45-B4-C27
A46-B4-C27
A47-B4-C27
A48-B4-C27
A49-B4-C27
A50-B4-C27
A51-B4-C27
A52-B4-C27
A53-B4-C27
A54-B4-C27
A55-B4-C27
A56-B4-C27
A57-B4-C27
A58-B4-C27
A59-B4-C27
A60-B4-C27
A61-B4-C27
A62-B4-C27
A63-B4-C27
A64-B4-C27
A65-B4-C27
A66-B4-C27
A67-B4-C27
A68-B4-C27
A69-B4-C27
A70-B4-C27
A71-B4-C27
A72-B4-C27
A73-B4-C27
A74-B4-C27
A75-B4-C27
A76-B4-C27
A77-B4-C27
A1-B1-C28
A2-B1-C28
A3-B1-C28
A4-B1-C28
A5-B1-C28
A6-B1-C28
A7-B1-C28
A8-B1-C28
A9-B1-C28
A10-B1-C28
A11-B1-C28
A12-B1-C28
A13-B1-C28
A14-B1-C28
A15-B1-C28
A16-B1-C28
A17-B1-C28
A18-B1-C28
A19-B1-C28
A20-B1-C28
A21-B1-C28
A22-B1-C28
A23-B1-C28
A24-B1-C28
A25-B1-C28
A26-B1-C28
A27-B1-C28
A28-B1-C28
A29-B1-C28
A30-B1-C28
A31-B1-C28
A32-B1-C28
A33-B1-C28
A34-B1-C28
A35-B1-C28
A36-B1-C28
A37-B1-C28
A38-B1-C28
A39-B1-C28
A40-B1-C28
A41-B1-C28
A42-B1-C28
A43-B1-C28
A44-B1-C28
A45-B1-C28
A46-B1-C28
A47-B1-C28
A48-B1-C28
A49-B1-C28
A50-B1-C28
A51-B1-C28
A52-B1-C28
A53-B1-C28
A54-B1-C28
A55-B1-C28
A56-B1-C28
A57-B1-C28
A58-B1-C28
A59-B1-C28
A60-B1-C28
A61-B1-C28
A62-B1-C28
A63-B1-C28
A64-B1-C28
A65-B1-C28
A66-B1-C28
A67-B1-C28
A68-B1-C28
A69-B1-C28
A70-B1-C28
A71-B1-C28
A72-B1-C28
A73-B1-C28
A74-B1-C28
A75-B1-C28
A76-B1-C28
A77-B1-C28
A1-B2-C28
A2-B2-C28
A3-B2-C28
A4-B2-C28
A5-B2-C28
A6-B2-C28
A7-B2-C28
A8-B2-C28
A9-B2-C28
A10-B2-C28
A11-B2-C28
A12-B2-C28
A13-B2-C28
A14-B2-C28
A15-B2-C28
A16-B2-C28
A17-B2-C28
A18-B2-C28
A19-B2-C28
A20-B2-C28
A21-B2-C28
A22-B2-C28
A23-B2-C28
A24-B2-C28
A25-B2-C28
A26-B2-C28
A27-B2-C28
A28-B2-C28
A29-B2-C28
A30-B2-C28
A31-B2-C28
A32-B2-C28
A33-B2-C28
A34-B2-C28
A35-B2-C28
A36-B2-C28
A37-B2-C28
A38-B2-C28
A39-B2-C28
A40-B2-C28
A41-B2-C28
A42-B2-C28
A43-B2-C28
A44-B2-C28
A45-B2-C28
A46-B2-C28
A47-B2-C28
A48-B2-C28
A49-B2-C28
A50-B2-C28
A51-B2-C28
A52-B2-C28
A53-B2-C28
A54-B2-C28
A55-B2-C28
A56-B2-C28
A57-B2-C28
A58-B2-C28
A59-B2-C28
A60-B2-C28
A61-B2-C28
A62-B2-C28
A63-B2-C28
A64-B2-C28
A65-B2-C28
A66-B2-C28
A67-B2-C28
A68-B2-C28
A69-B2-C28
A70-B2-C28
A71-B2-C28
A72-B2-C28
A73-B2-C28
A74-B2-C28
A75-B2-C28
A76-B2-C28
A77-B2-C28
A1-B3-C28
A2-B3-C28
A3-B3-C28
A4-B3-C28
A5-B3-C28
A6-B3-C28
A7-B3-C28
A8-B3-C28
A9-B3-C28
A10-B3-C28
A11-B3-C28
A12-B3-C28
A13-B3-C28
A14-B3-C28
A15-B3-C28
A16-B3-C28
A17-B3-C28
A18-B3-C28
A19-B3-C28
A20-B3-C28
A21-B3-C28
A22-B3-C28
A23-B3-C28
A24-B3-C28
A25-B3-C28
A26-B3-C28
A27-B3-C28
A28-B3-C28
A29-B3-C28
A30-B3-C28
A31-B3-C28
A32-B3-C28
A33-B3-C28
A34-B3-C28
A35-B3-C28
A36-B3-C28
A37-B3-C28
A38-B3-C28
A39-B3-C28
A40-B3-C28
A41-B3-C28
A42-B3-C28
A43-B3-C28
A44-B3-C28
A45-B3-C28
A46-B3-C28

A47-B3-C28
A48-B3-C28
A49-B3-C28
A50-B3-C28
A51-B3-C28
A52-B3-C28
A53-B3-C28
A54-B3-C28
A55-B3-C28
A56-B3-C28
A57-B3-C28
A58-B3-C28
A59-B3-C28
A60-B3-C28
A61-B3-C28
A62-B3-C28
A63-B3-C28
A64-B3-C28
A65-B3-C28
A66-B3-C28
A67-B3-C28
A68-B3-C28
A69-B3-C28
A70-B3-C28
A71-B3-C28
A72-B3-C28
A73-B3-C28
A74-B3-C28
A75-B3-C28
A76-B3-C28
A77-B3-C28
A1-B4-C28
A2-B4-C28
A3-B4-C28
A4-B4-C28
A5-B4-C28
A6-B4-C28
A7-B4-C28
A8-B4-C28
A9-B4-C28
A10-B4-C28
A11-B4-C28
A12-B4-C28
A13-B4-C28
A14-B4-C28
A15-B4-C28
A16-B4-C28
A17-B4-C28
A18-B4-C28
A19-B4-C28
A20-B4-C28
A21-B4-C28
A22-B4-C28
A23-B4-C28
A24-B4-C28
A25-B4-C28
A26-B4-C28
A27-B4-C28
A28-B4-C28
A29-B4-C28
A30-B4-C28
A31-B4-C28
A32-B4-C28
A33-B4-C28
A34-B4-C28
A35-B4-C28
A36-B4-C28
A37-B4-C28
A38-B4-C28
A39-B4-C28
A40-B4-C28
A41-B4-C28
A42-B4-C28
A43-B4-C28
A44-B4-C28
A45-B4-C28
A46-B4-C28
A47-B4-C28
A48-B4-C28
A49-B4-C28
A50-B4-C28
A51-B4-C28
A52-B4-C28
A53-B4-C28
A54-B4-C28
A55-B4-C28
A56-B4-C28
A57-B4-C28
A58-B4-C28
A59-B4-C28
A60-B4-C28
A61-B4-C28
A62-B4-C28
A63-B4-C28
A64-B4-C28
A65-B4-C28
A66-B4-C28
A67-B4-C28
A68-B4-C28
A69-B4-C28
A70-B4-C28
A71-B4-C28
A72-B4-C28
A73-B4-C28
A74-B4-C28
A75-B4-C28
A76-B4-C28
A77-B4-C28
A1-B1-C29
A2-B1-C29
A3-B1-C29
A4-B1-C29
A5-B1-C29
A6-B1-C29
A7-B1-C29
A8-B1-C29
A9-B1-C29
A10-B1-C29
A11-B1-C29
A12-B1-C29
A13-B1-C29
A14-B1-C29
A15-B1-C29
A16-B1-C29
A17-B1-C29
A18-B1-C29
A19-B1-C29
A20-B1-C29
A21-B1-C29
A22-B1-C29
A23-B1-C29
A24-B1-C29
A25-B1-C29
A26-B1-C29
A27-B1-C29
A28-B1-C29
A29-B1-C29
A30-B1-C29
A31-B1-C29
A32-B1-C29
A33-B1-C29
A34-B1-C29
A35-B1-C29
A36-B1-C29
A37-B1-C29
A38-B1-C29
A39-B1-C29
A40-B1-C29
A41-B1-C29
A42-B1-C29
A43-B1-C29
A44-B1-C29
A45-B1-C29
A46-B1-C29
A47-B1-C29
A48-B1-C29
A49-B1-C29
A50-B1-C29
A51-B1-C29
A52-B1-C29
A53-B1-C29
A54-B1-C29
A55-B1-C29
A56-B1-C29
A57-B1-C29
A58-B1-C29
A59-B1-C29
A60-B1-C29
A61-B1-C29
A62-B1-C29
A63-B1-C29
A64-B1-C29
A65-B1-C29
A66-B1-C29
A67-B1-C29
A68-B1-C29
A69-B1-C29
A70-B1-C29
A71-B1-C29
A72-B1-C29
A73-B1-C29
A74-B1-C29
A75-B1-C29
A76-B1-C29
A77-B1-C29
A1-B2-C29
A2-B2-C29
A3-B2-C29
A4-B2-C29
A5-B2-C29
A6-B2-C29
A7-B2-C29
A8-B2-C29
A9-B2-C29
A10-B2-C29
A11-B2-C29
A12-B2-C29
A13-B2-C29
A14-B2-C29
A15-B2-C29
A16-B2-C29
A17-B2-C29
A18-B2-C29
A19-B2-C29
A20-B2-C29
A21-B2-C29
A22-B2-C29
A23-B2-C29
A24-B2-C29
A25-B2-C29
A26-B2-C29
A27-B2-C29
A28-B2-C29
A29-B2-C29
A30-B2-C29
A31-B2-C29
A32-B2-C29
A33-B2-C29
A34-B2-C29
A35-B2-C29
A36-B2-C29
A37-B2-C29
A38-B2-C29
A39-B2-C29
A40-B2-C29
A41-B2-C29
A42-B2-C29
A43-B2-C29
A44-B2-C29
A45-B2-C29
A46-B2-C29
A47-B2-C29
A48-B2-C29
A49-B2-C29
A50-B2-C29
A51-B2-C29
A52-B2-C29
A53-B2-C29
A54-B2-C29
A55-B2-C29
A56-B2-C29
A57-B2-C29
A58-B2-C29
A59-B2-C29
A60-B2-C29
A61-B2-C29
A62-B2-C29
A63-B2-C29
A64-B2-C29
A65-B2-C29
A66-B2-C29
A67-B2-C29
A68-B2-C29
A69-B2-C29
A70-B2-C29
A71-B2-C29
A72-B2-C29
A73-B2-C29
A74-B2-C29
A75-B2-C29
A76-B2-C29
A77-B2-C29
A1-B3-C29
A2-B3-C29

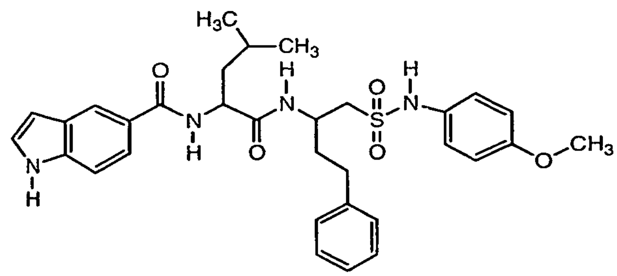
A3-B3-C29
A4-B3-C29
A5-B3-C29
A6-B3-C29
A7-B3-C29
A8-B3-C29
A9-B3-C29
A10-B3-C29
A11-B3-C29
A12-B3-C29
A13-B3-C29
A14-B3-C29
A15-B3-C29
A16-B3-C29
A17-B3-C29
A18-B3-C29
A19-B3-C29
A20-B3-C29
A21-B3-C29
A22-B3-C29
A23-B3-C29
A24-B3-C29
A25-B3-C29
A26-B3-C29
A27-B3-C29
A28-B3-C29
A29-B3-C29
A30-B3-C29
A31-B3-C29
A32-B3-C29
A33-B3-C29
A34-B3-C29
A35-B3-C29
A36-B3-C29
A37-B3-C29
A38-B3-C29
A39-B3-C29
A40-B3-C29
A41-B3-C29
A42-B3-C29
A43-B3-C29
A44-B3-C29
A45-B3-C29
A46-B3-C29
A47-B3-C29
A48-B3-C29
A49-B3-C29
A50-B3-C29
A51-B3-C29
A52-B3-C29
A53-B3-C29
A54-B3-C29
A55-B3-C29
A56-B3-C29
A57-B3-C29
A58-B3-C29
A59-B3-C29
A60-B3-C29
A61-B3-C29
A62-B3-C29
A63-B3-C29
A64-B3-C29
A65-B3-C29
A66-B3-C29
A67-B3-C29
A68-B3-C29
A69-B3-C29
A70-B3-C29
A71-B3-C29
A72-B3-C29
A73-B3-C29
A74-B3-C29
A75-B3-C29
A76-B3-C29
A77-B3-C29
A1-B4-C29
A2-B4-C29
A3-B4-C29
A4-B4-C29
A5-B4-C29
A6-B4-C29
A7-B4-C29
A8-B4-C29
A9-B4-C29
A10-B4-C29
A11-B4-C29
A12-B4-C29
A13-B4-C29
A14-B4-C29
A15-B4-C29
A16-B4-C29
A17-B4-C29
A18-B4-C29
A19-B4-C29
A20-B4-C29
A21-B4-C29
A22-B4-C29
A23-B4-C29
A24-B4-C29
A25-B4-C29
A26-B4-C29
A27-B4-C29
A28-B4-C29
A29-B4-C29
A30-B4-C29
A31-B4-C29
A32-B4-C29
A33-B4-C29
A34-B4-C29
A35-B4-C29
A36-B4-C29
A37-B4-C29
A38-B4-C29
A39-B4-C29
A40-B4-C29
A41-B4-C29
A42-B4-C29
A43-B4-C29
A44-B4-C29
A45-B4-C29
A46-B4-C29
A47-B4-C29
A48-B4-C29
A49-B4-C29
A50-B4-C29
A51-B4-C29
A52-B4-C29
A53-B4-C29
A54-B4-C29
A55-B4-C29
A56-B4-C29
A57-B4-C29
A58-B4-C29
A59-B4-C29
A60-B4-C29
A61-B4-C29
A62-B4-C29
A63-B4-C29
A64-B4-C29
A65-B4-C29
A66-B4-C29
A67-B4-C29
A68-B4-C29
A69-B4-C29
A70-B4-C29
A71-B4-C29
A72-B4-C29
A73-B4-C29
A74-B4-C29
A75-B4-C29
A76-B4-C29
A77-B4-C29
A1-B1-C30
A2-B1-C30
A3-B1-C30
A4-B1-C30
A5-B1-C30
A6-B1-C30
A7-B1-C30
A8-B1-C30
A9-B1-C30
A10-B1-C30
A11-B1-C30
A12-B1-C30
A13-B1-C30
A14-B1-C30
A15-B1-C30
A16-B1-C30
A17-B1-C30
A18-B1-C30
A19-B1-C30
A20-B1-C30
A21-B1-C30
A22-B1-C30
A23-B1-C30
A24-B1-C30
A25-B1-C30
A26-B1-C30
A27-B1-C30
A28-B1-C30
A29-B1-C30
A30-B1-C30
A31-B1-C30
A32-B1-C30
A33-B1-C30
A34-B1-C30
A35-B1-C30
A36-B1-C30
A37-B1-C30
A38-B1-C30
A39-B1-C30
A40-B1-C30
A41-B1-C30
A42-B1-C30
A43-B1-C30
A44-B1-C30
A45-B1-C30
A46-B1-C30
A47-B1-C30
A48-B1-C30
A49-B1-C30
A50-B1-C30
A51-B1-C30
A52-B1-C30
A53-B1-C30
A54-B1-C30
A55-B1-C30
A56-B1-C30
A57-B1-C30
A58-B1-C30
A59-B1-C30
A60-B1-C30
A61-B1-C30
A62-B1-C30
A63-B1-C30
A64-B1-C30
A65-B1-C30
A66-B1-C30
A67-B1-C30
A68-B1-C30
A69-B1-C30
A70-B1-C30
A71-B1-C30
A72-B1-C30
A73-B1-C30
A74-B1-C30
A75-B1-C30
A76-B1-C30
A77-B1-C30
A1-B2-C30
A2-B2-C30
A3-B2-C30
A4-B2-C30
A5-B2-C30
A6-B2-C30
A7-B2-C30
A8-B2-C30
A9-B2-C30
A10-B2-C30
A11-B2-C30
A12-B2-C30
A13-B2-C30
A14-B2-C30
A15-B2-C30
A16-B2-C30
A17-B2-C30
A18-B2-C30
A19-B2-C30
A20-B2-C30
A21-B2-C30
A22-B2-C30
A23-B2-C30
A24-B2-C30
A25-B2-C30
A26-B2-C30
A27-B2-C30
A28-B2-C30
A29-B2-C30
A30-B2-C30
A31-B2-C30
A32-B2-C30
A33-B2-C30
A34-B2-C30
A35-B2-C30

A36-B2-C30
A37-B2-C30
A38-B2-C30
A39-B2-C30
A40-B2-C30
A41-B2-C30
A42-B2-C30
A43-B2-C30
A44-B2-C30
A45-B2-C30
A46-B2-C30
A47-B2-C30
A48-B2-C30
A49-B2-C30
A50-B2-C30
A51-B2-C30
A52-B2-C30
A53-B2-C30
A54-B2-C30
A55-B2-C30
A56-B2-C30
A57-B2-C30
A58-B2-C30
A59-B2-C30
A60-B2-C30
A61-B2-C30
A62-B2-C30
A63-B2-C30
A64-B2-C30
A65-B2-C30
A66-B2-C30
A67-B2-C30
A68-B2-C30
A69-B2-C30
A70-B2-C30
A71-B2-C30
A72-B2-C30
A73-B2-C30
A74-B2-C30
A75-B2-C30
A76-B2-C30
A77-B2-C30
A1-B3-C30
A2-B3-C30
A3-B3-C30
A4-B3-C30
A5-B3-C30
A6-B3-C30
A7-B3-C30
A8-B3-C30
A9-B3-C30
A10-B3-C30
A11-B3-C30
A12-B3-C30
A13-B3-C30
A14-B3-C30
A15-B3-C30
A16-B3-C30
A17-B3-C30
A18-B3-C30
A19-B3-C30
A20-B3-C30
A21-B3-C30
A22-B3-C30
A23-B3-C30
A24-B3-C30
A25-B3-C30
A26-B3-C30
A27-B3-C30
A28-B3-C30
A29-B3-C30
A30-B3-C30
A31-B3-C30
A32-B3-C30
A33-B3-C30
A34-B3-C30
A35-B3-C30
A36-B3-C30
A37-B3-C30
A38-B3-C30
A39-B3-C30
A40-B3-C30
A41-B3-C30
A42-B3-C30
A43-B3-C30
A44-B3-C30
A45-B3-C30
A46-B3-C30
A47-B3-C30
A48-B3-C30
A49-B3-C30
A50-B3-C30
A51-B3-C30
A52-B3-C30
A53-B3-C30
A54-B3-C30
A55-B3-C30
A56-B3-C30
A57-B3-C30
A58-B3-C30
A59-B3-C30
A60-B3-C30
A61-B3-C30
A62-B3-C30
A63-B3-C30
A64-B3-C30
A65-B3-C30
A66-B3-C30
A67-B3-C30
A68-B3-C30
A69-B3-C30
A70-B3-C30
A71-B3-C30
A72-B3-C30
A73-B3-C30
A74-B3-C30
A75-B3-C30
A76-B3-C30
A77-B3-C30
A1-B4-C30
A2-B4-C30
A3-B4-C30
A4-B4-C30
A5-B4-C30
A6-B4-C30
A7-B4-C30
A8-B4-C30
A9-B4-C30
A10-B4-C30
A11-B4-C30
A12-B4-C30
A13-B4-C30
A14-B4-C30
A15-B4-C30
A16-B4-C30
A17-B4-C30
A18-B4-C30
A19-B4-C30
A20-B4-C30
A21-B4-C30
A22-B4-C30
A23-B4-C30
A24-B4-C30
A25-B4-C30
A26-B4-C30
A27-B4-C30
A28-B4-C30
A29-B4-C30
A30-B4-C30
A31-B4-C30
A32-B4-C30
A33-B4-C30
A34-B4-C30
A35-B4-C30
A36-B4-C30
A37-B4-C30
A38-B4-C30
A39-B4-C30
A40-B4-C30
A41-B4-C30
A42-B4-C30
A43-B4-C30
A44-B4-C30
A45-B4-C30
A46-B4-C30
A47-B4-C30
A48-B4-C30
A49-B4-C30
A50-B4-C30
A51-B4-C30
A52-B4-C30
A53-B4-C30
A54-B4-C30
A55-B4-C30
A56-B4-C30
A57-B4-C30
A58-B4-C30
A59-B4-C30
A60-B4-C30
A61-B4-C30
A62-B4-C30
A63-B4-C30
A64-B4-C30
A65-B4-C30
A66-B4-C30
A67-B4-C30
A68-B4-C30
A69-B4-C30
A70-B4-C30
A71-B4-C30
A72-B4-C30
A73-B4-C30
A74-B4-C30
A75-B4-C30
A76-B4-C30
A77-B4-C30
A1-B1-C31
A2-B1-C31
A3-B1-C31
A4-B1-C31
A5-B1-C31
A6-B1-C31
A7-B1-C31
A8-B1-C31
A9-B1-C31
A10-B1-C31
A11-B1-C31
A12-B1-C31
A13-B1-C31
A14-B1-C31
A15-B1-C31
A16-B1-C31
A17-B1-C31
A18-B1-C31
A19-B1-C31
A20-B1-C31
A21-B1-C31
A22-B1-C31
A23-B1-C31
A24-B1-C31
A25-B1-C31
A26-B1-C31
A27-B1-C31
A28-B1-C31
A29-B1-C31
A30-B1-C31
A31-B1-C31
A32-B1-C31
A33-B1-C31
A34-B1-C31
A35-B1-C31
A36-B1-C31
A37-B1-C31
A38-B1-C31
A39-B1-C31
A40-B1-C31
A41-B1-C31
A42-B1-C31
A43-B1-C31
A44-B1-C31
A45-B1-C31
A46-B1-C31
A47-B1-C31
A48-B1-C31
A49-B1-C31
A50-B1-C31
A51-B1-C31
A52-B1-C31
A53-B1-C31
A54-B1-C31
A55-B1-C31
A56-B1-C31
A57-B1-C31
A58-B1-C31
A59-B1-C31
A60-B1-C31
A61-B1-C31
A62-B1-C31
A63-B1-C31
A64-B1-C31
A65-B1-C31
A66-B1-C31
A67-B1-C31
A68-B1-C31

A69-B1-C31
A70-B1-C31
A71-B1-C31
A72-B1-C31
A73-B1-C31
A74-B1-C31
A75-B1-C31
A76-B1-C31
A77-B1-C31
A1-B2-C31
A2-B2-C31
A3-B2-C31
A4-B2-C31
A5-B2-C31
A6-B2-C31
A7-B2-C31
A8-B2-C31
A9-B2-C31
A10-B2-C31
A11-B2-C31
A12-B2-C31
A13-B2-C31
A14-B2-C31
A15-B2-C31
A16-B2-C31
A17-B2-C31
A18-B2-C31
A19-B2-C31
A20-B2-C31
A21-B2-C31
A22-B2-C31
A23-B2-C31
A24-B2-C31
A25-B2-C31
A26-B2-C31
A27-B2-C31
A28-B2-C31
A29-B2-C31
A30-B2-C31
A31-B2-C31
A32-B2-C31
A33-B2-C31
A34-B2-C31
A35-B2-C31
A36-B2-C31
A37-B2-C31
A38-B2-C31
A39-B2-C31
A40-B2-C31
A41-B2-C31
A42-B2-C31
A43-B2-C31
A44-B2-C31
A45-B2-C31
A46-B2-C31
A47-B2-C31
A48-B2-C31
A49-B2-C31
A50-B2-C31
A51-B2-C31
A52-B2-C31
A53-B2-C31
A54-B2-C31
A55-B2-C31
A56-B2-C31
A57-B2-C31
A58-B2-C31
A59-B2-C31
A60-B2-C31
A61-B2-C31
A62-B2-C31
A63-B2-C31
A64-B2-C31
A65-B2-C31
A66-B2-C31
A67-B2-C31
A68-B2-C31
A69-B2-C31
A70-B2-C31
A71-B2-C31
A72-B2-C31
A73-B2-C31
A74-B2-C31
A75-B2-C31
A76-B2-C31
A77-B2-C31
A1-B3-C31
A2-B3-C31
A3-B3-C31
A4-B3-C31
A5-B3-C31
A6-B3-C31
A7-B3-C31
A8-B3-C31
A9-B3-C31
A10-B3-C31
A11-B3-C31
A12-B3-C31
A13-B3-C31
A14-B3-C31
A15-B3-C31
A16-B3-C31
A17-B3-C31
A18-B3-C31
A19-B3-C31
A20-B3-C31
A21-B3-C31
A22-B3-C31
A23-B3-C31
A24-B3-C31
A25-B3-C31
A26-B3-C31
A27-B3-C31
A28-B3-C31
A29-B3-C31
A30-B3-C31
A31-B3-C31
A32-B3-C31
A33-B3-C31
A34-B3-C31
A35-B3-C31
A36-B3-C31
A37-B3-C31
A38-B3-C31
A39-B3-C31
A40-B3-C31
A41-B3-C31
A42-B3-C31
A43-B3-C31
A44-B3-C31
A45-B3-C31
A46-B3-C31
A47-B3-C31
A48-B3-C31
A49-B3-C31
A50-B3-C31
A51-B3-C31
A52-B3-C31
A53-B3-C31
A54-B3-C31
A55-B3-C31
A56-B3-C31
A57-B3-C31
A58-B3-C31
A59-B3-C31
A60-B3-C31
A61-B3-C31
A62-B3-C31
A63-B3-C31
A64-B3-C31
A65-B3-C31
A66-B3-C31
A67-B3-C31
A68-B3-C31
A69-B3-C31
A70-B3-C31
A71-B3-C31
A72-B3-C31
A73-B3-C31
A74-B3-C31
A75-B3-C31
A76-B3-C31
A77-B3-C31
A1-B4-C31
A2-B4-C31
A3-B4-C31
A4-B4-C31
A5-B4-C31
A6-B4-C31
A7-B4-C31
A8-B4-C31
A9-B4-C31
A10-B4-C31
A11-B4-C31
A12-B4-C31
A13-B4-C31
A14-B4-C31
A15-B4-C31
A16-B4-C31
A17-B4-C31
A18-B4-C31
A19-B4-C31
A20-B4-C31
A21-B4-C31
A22-B4-C31
A23-B4-C31
A24-B4-C31
A25-B4-C31
A26-B4-C31
A27-B4-C31
A28-B4-C31
A29-B4-C31
A30-B4-C31
A31-B4-C31
A32-B4-C31
A33-B4-C31
A34-B4-C31
A35-B4-C31
A36-B4-C31
A37-B4-C31
A38-B4-C31
A39-B4-C31
A40-B4-C31
A41-B4-C31
A42-B4-C31
A43-B4-C31
A44-B4-C31
A45-B4-C31
A46-B4-C31
A47-B4-C31
A48-B4-C31
A49-B4-C31
A50-B4-C31
A51-B4-C31
A52-B4-C31
A53-B4-C31
A54-B4-C31
A55-B4-C31
A56-B4-C31
A57-B4-C31
A58-B4-C31
A59-B4-C31
A60-B4-C31
A61-B4-C31
A62-B4-C31
A63-B4-C31
A64-B4-C31
A65-B4-C31
A66-B4-C31
A67-B4-C31
A68-B4-C31
A69-B4-C31
A70-B4-C31
A71-B4-C31
A72-B4-C31
A73-B4-C31
A74-B4-C31
A75-B4-C31
A76-B4-C31
A77-B4-C31

Thus, for example, in table 4 the compound denoted as A60-B1-C7 is the product of the combination of group A60 in Table 1 and B1 in Table 2 and C7 in Table 3, namely 1H-indole-5-

carboxylic acid (1-{1-[(4-methoxy-phenylsulfamoyl)-methyl]-3-phenyl-propylcarbamoyl}-3-methyl-butyl)-amide:



Further preferred are compounds selected from the group consisting of:

benzyl (1S-{1S-[(4-methoxyphenylsulfamoyl)-methyl]-3-phenyl-propylcarbamoyl}-3-methyl-butyl)-carbamate (Compound 1);

benzyl (1S-{1S-[(4-methoxyphenylsulfamoyl)-methyl]-3-phenyl-propylcarbamoyl}-2-methyl-butyl)-carbamate (Compound 2);

tert-butyl (1S-{1S-[(4-methoxyphenylsulfamoyl)-methyl]-3-phenyl-propylcarbamoyl}-3-methyl-butyl)-carbamate (Compound 3);

benzyl (1S-{1S-[(3-acetyl-phenylsulfamoyl)-methyl]-3-phenyl-propylcarbamoyl}-3-methyl-butyl)-carbamate (Compound 4);

N-{1*S*-[1*S*-(4-methoxyphenylsulfamoylmethyl)-3-phenylpropylcarbamoyl]-2-methylbutyl}-4-methylpiperazine-1-carboxamide (Compound 5);

benzyl {1S-[2-(4-methoxyphenylsulfamoyl)-ethylcarbamoyl]-2-methyl-butyl}-carbamate (Compound 6);

(2-cyclohexyl-1S-{3-phenyl-1S-[(2-phenylaminoethylsulfamoyl)-methyl]-propylcarbamoyl}ethyl)-carbamic acid *tert*-butyl ester (Compound 7);

4-dimethylamino-N-(1S-{1S-[(4-methoxyphenylsulfamoyl)methyl]-3-phenyl-propylcarbamoyl}-3-methylbutyl)-benzamide(Compound 8);

quinoline-6-carboxylic acid (1S-{1S-[(4-methoxyphenylsulfamoyl)methyl]-3-phenyl-propylcarbamoyl}-3-methyl-butyl)-amide (Compound 9);

morpholine-4-carboxylic acid (2-cyclohexyl-1S-{3-phenyl-1S-[(2-phenylamino-ethylsulfamoyl)methyl]-propylcarbamoyl}-ethyl)-amide (Compound 10);

4-(2-dimethylaminothiazol-4-yl)-N-{1S-[2-(4-methoxyphenylsulfamoyl)-ethylcarbamoyl]-3-methyl-butyl}benzamide (Compound 11);

2S-acetylamino-3-cyclohexyl-N-{1-[(4-methoxyphenylsulfamoyl)-methyl]-3-phenyl-propyl}propionamide (Compound 12);

2R-acetylamino-3-cyclohexyl-N-{1-[(4-methoxyphenylsulfamoyl)methyl]-3-phenyl-propyl}propionamide (Compound 13);

2RS-acetylamino-3-cyclohexyl-N-{1-[(4-hydroxyphenylsulfamoyl)methyl]-3-phenyl-propyl}-propionamide (Compound 14);

benzyl [6-(4-methoxyphenylsulfamoyl)-5S-(4-methyl-2S-{4-[2-(pyridin-3-ylamino)thiazol-4-yl]-benzoylamino}pentanoylamino)hexyl]carbamate (Compound 15);

N-(1S-{1S-[(4-methoxyphenylsulfamoyl)methyl]-3-phenylpropylcarbamoyl}-3-methyl-butyl)-4-[2-(pyridin-3-ylamino)thiazol-4-yl]-benzamide (Compound 16);

N-(1S-{1S-[(4-methoxyphenylsulfamoyl)methyl]-3-phenyl-propylcarbamoyl}-3-methyl-butyl)-nicotinamide (Compound 19);

N-(1S-{1S-[(4-methoxyphenylsulfamoyl)-methyl]-3-phenylpropylcarbamoyl}-3-methyl-butyl)-isonicotinamide (Compound 20);

N-{1-[1-(4-methoxyphenylsulfamoylmethyl)-3-phenylpropylcarbamoyl]-3-methylbutyl}-1*H*-indole-5-carboxamide (Compound 21);

tert-butyl [3-(1S-{1S-[(4-methoxyphenylsulfamoyl)-methyl]-3-phenylpropylcarbamoyl}-3-methyl-butylcarbamoyl)phenyl]-carbamate (Compound 22);

3-amino-N-(1S-{1S-[(4-methoxyphenylsulfamoyl)-methyl]-3-phenylpropylcarbamoyl}-3-methyl-butyl)-benzamide (Compound 23);

N-(1S-{5-amino-1S-[(4-methoxyphenylsulfamoyl)methyl]pentylcarbamoyl}-3-methyl-butyl)-4-[2-(pyridin-3-ylamino)-thiazol-4-yl]-benzamide (Compound 24);

benzyl [1S-(1S-{[3-(1-hydroxyethyl)phenylsulfamoyl]methyl}-3-phenylpropyl-carbamoyl)-3-methylbutyl]-carbamate (Compound 26);

morpholine 4-carboxylic acid (1S-{5-amino-1S-[(4-methoxyphenylsulfamoyl)methyl]-pentylcarbamoyl}-2-phenylmethanesulfonylethyl)amide;

(5S-[2S-(morpholin-4-ylcarbonyl)amino]-3-phenylmethanesulfonylpropionylamino}-6-phenylsulfamoylhexyl)carbamic acid benzyl ester;

morpholine 4-carboxylic acid (1S-{1S-[(4-methoxyphenylsulfamoyl)methyl]-3-phenylpropylcarbamoyl}-2-phenylmethanesulfonylethyl)amide;

N-(1S-{1S-[(4-methoxy-phenylsulfamoyl)-methyl]-3-phenyl-propylcarbamoyl}-cyclohexyl)-4-[2-(4-methylpiperazin-1-yl)thiazol-4-yl]benzamide; and

N-(1S-{1S-[(4-methoxy-phenylsulfamoyl)-methyl]-3-phenyl-propylcarbamoyl}-

cyclohexyl)-4-(4-propylpiperazin-1-yl)-benzamide.

The names of these compounds were generated using Autonom Version 2.1 or 4.0.

GENERAL SYNTHESIS

Compounds of this invention can be made by the methods depicted in the reaction schemes shown below.

The starting materials and reagents used in preparing these compounds are either available from commercial suppliers such as Aldrich Chemical Co., (Milwaukee, Wis.), or Bachem (Torrance, Calif.), or are prepared by methods known to those skilled in the art following procedures set forth in references such as Fieser and Fieser's Reagents for Organic Synthesis, Volumes 1-17 (John Wiley and Sons, 1991); Rodd's Chemistry of Carbon Compounds, Volumes 1-5 and Supplementals (Elsevier Science Publishers, 1989); Organic Reactions, Volumes 1-40 (John Wiley and Sons, 1991), March's Advanced Organic Chemistry, (John Wiley and Sons, 4th Edition) and Larock's Comprehensive Organic Transformations (VCH Publishers Inc., 1989). These schemes are merely illustrative of some methods by which the compounds of this invention can be synthesized, and various modifications to these schemes can be made and will be suggested to one skilled in the art having referred to this disclosure.

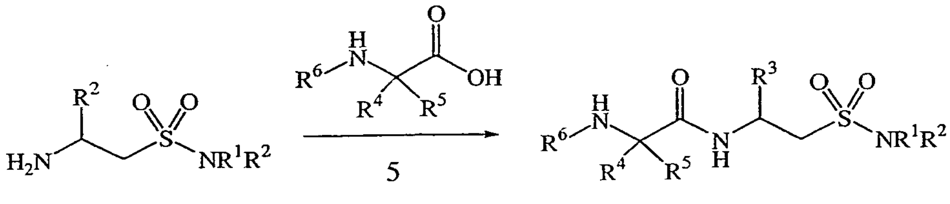
The starting materials and the intermediates of the reaction may be isolated and purified if desired using conventional techniques, including but not limited to filtration, distillation, crystallization, chromatography and the like. Such materials may be characterized using conventional means, including physical constants and spectral data.

Unless specified to the contrary, the reactions described herein take place at atmospheric pressure over a temperature range from about –78° C. to about 150° C., more preferably from about 0° C. to about 125° C. and most preferably at about room (or ambient) temperature, e.g., about 20° C.

Compounds of Formula I can be prepared by the procedure illustrated and described in Schemes 1 and 2 below:

Compounds of Formula I in which R^1, R^2, R^3, R^4, R^5 and R^6 are as defined in the Summary of the Invention can be prepared by proceeding as in the following Scheme 1 below.

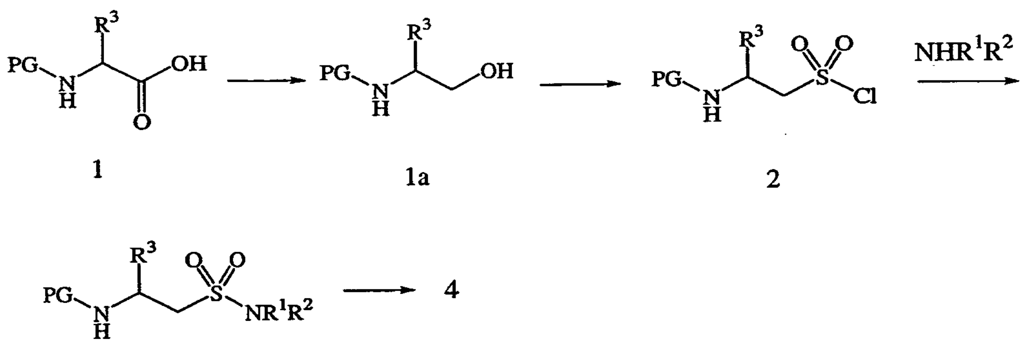
Scheme 1



4 I

Compounds of Formula I can be prepared by condensing a compound of formula 4 with a compound of formula 5. The compound of formula 4 may be in a free base or an acid addition salt form, preferably an acid addition salt form (e.g. *p*-toluenesulfonic acid salt, or the like). Typically, the condensation reaction is carried out under nitrogen in the presence of a suitable condensing agent (e.g. isobutyl chloroformate, PyBOP, HATU, or the like), a non-nucleophilic base (e.g. 4-methylmorpholine, triethylamine, or the like) and a suitable solvent (e.g., THF, DMF, or the like), at -20 to 0 °C, preferably at about –10 °C, and requires 45 minutes to 12 hours to complete. A detailed description of the condensation reaction is found in the Examples, *infra*.

Compounds of formula 4 in which R^3 is as defined in the Summary of the Invention for Formula I can be prepared as illustrated and described below.



1 1a 2 3

Treatment of an N-protected alpha amino acid compound of formula 1 with a condensing agent (e.g., isobutyl chloroformate, or the like) in the presence of a suitable base (e.g., 4-methylmorpholine, or the like) in a suitable solvent (e.g., THF, etc.) at a temperature of about -10 to 10 °C, preferably 0 °C, for about 5 to 20 hours, followed by reaction of the resulting anhydride intermediate with a suitable reducing agent (e.g., sodium borohydride, and the like) provides a 2-N-protected aminoethanol intermediate of formula 1a. Compounds of formula 1 are commercially available or they can be prepared by methods well known in the

art.

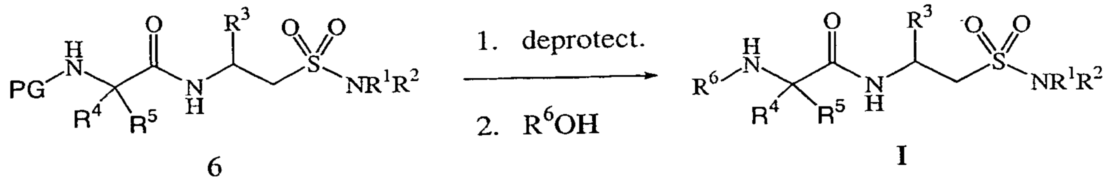
Treatment of 1a with an alkylsulfonyl halide (e.g., methanesulfonylchloride, or the like) in the presence of a suitable base (e.g., triethylamine, etc.) and in a suitable solvent (e.g., DCM, and the like) and at a temperature of about -10 to 10°C, preferably 0 °C, for about 5 to 20 hours provides the corresponding alkylsulfonyloxy derivative. Treatment of the alkylsulfonyloxy derivative with an acylating agent (e.g., cesium thiolacetate, or the like) in a suitable solvent (e.g., DMF, and the like) and at a temperature of about 10 to 30 °C, preferably 20°C, for about 5 to 20 hours provides a thioester which upon reaction with chlorine gas in a suitable solvent (e.g., DCM, and the like) at a temperature of about 10 to 30°C, preferably 20°C, for about 15 minutes to about 2 hours provides a compound of formula 2.

Compounds of formula 3 can be prepared by reacting a compound of formula 2 with an amine of the formula NHR^1R^2 and then removing the protecting group (PG) to yield a compound of formula 4. Typically, the reaction with the amine is carried out in the presence of a suitable solvent (e.g., DCM, or the like) and at a temperature of about -10 to 10°C, preferably 0°C, for about 5 to 20 hours. Deprotection can be effected by any means that removes the protecting group and gives the desired product in reasonable yield. For example, when the protecting group is *t*-butoxycarbonyl, deprotecting can be effected with a suitable anhydrous acid (e.g., anhydrous hydrogen chloride, anhydrous *p*-toluenesulfonic acid, or the like) at ambient temperature for about 12 to 24 hours.

Compounds of formula 5 are either commercially available or they can be prepared by methods well known in the art. For examples, t-BOC alanine, t-BOC-leucine, t-BOC-isoleucine are commercially available. Compounds of formula 5 where R^6 is other groups within the scope of the invention sacan be readily prepared commercially available alpha amino acids by methods well known in the art. Some such methods are disclosed in US Patent 6,136,844 the disclosure of which is incorporated by reference in its entirety.

Compounds of Formula I in which R^1, R^2, R^3, R^4, R^5 and R^6 are as defined in the Summary of the Invention can also be prepared from compounds of formula 6 as illustrated and described in Scheme 2 below.

Scheme 2



Compounds of Formula I can also be prepared by deprotecting a compound of formula 6 and then treating the resulting free amine with an acid of formula R^6OH or its acid derivative such as acid chloride. The compound of formula 6 may be in a free base or an acid addition salt form, preferably an acid addition salt form (e.g. *p*-toluenesulfonic acid salt, or the like).

Deprotection can be effected by any means that removes the protecting group and gives the desired product in reasonable yield. A detailed description of the techniques applicable to the creation of protective groups and their removal can be found in T.W. Greene and P.G.M. Wuts, *Protective Groups in Organic Synthesis*, John Wiley & Sons, Inc. (3rd Edition) 1999. For example, when the protecting group is BOC, deprotection can be effected by treating with anhydrous hydrogen chloride in a suitable solvent (e.g., dichloromethane, diethyl ether, dioxane, or the like), at 10 to 30°C, preferably at about 20°C, and requires about 5 to 10 hours to complete. A detailed description of the deprotection reaction is found in Example 5, *infra*.

The reaction conditions employed for the coupling of the free amine of compound 6 with R^6OH depend on the nature of R^6OH. For example, if an acid is used, then the reaction is carried out in the presence of a coupling agent such as PyBOP as described in Scheme 1 above. If an acid chloride is used then the reaction is carried out in the presence of a base such as triethylamine, pyridine, and the like and in a suitable organic solvent such as tetrahydrofuran, methylene chloride, and the like.

The reaction can be carried out at temperatures from about 10 to about 30°C, preferably at about 20°C, and requires 3 to 20 hours to complete. A detailed description of the step 2 reaction is found in the Examples, *infra*.

Additional Processes for Preparing Compounds of Formula I:

Compounds of Formula I in which R^6 is hydrogen can be prepared by deacylating a compound of Formula I in which R^6 is $-X^3X^4R^{13}$. For example, deacylation of a compound of Formula I in which R^5 is *t*-butyloxycarbonyl or benzyloxycarbonyl can be effected by treating with anhydrous hydrogen chloride or hydrogen bromide in a suitable solvent (e.g., DCM, dioxane, glacial acetic acid, or the like) at 10 to 30°C, preferable at about 20°C, for 5 to 20 hours. A detailed description of the reaction is found in the Examples, *infra*.

Compounds of Formula I can be further treated with a reducing agent (e.g., $NaBH_4$, $LiALH_4$, or the like), in the presence of a suitable solvent (e.g., tetrahydrofuran (THF), dimethylformamide (DMF) or the like), at 10 to 30°C, preferably at about 20°C, and requires 15 minutes to 2 hours to complete. A detailed description of the reduction reaction is found in the Examples, *infra*.

A compound of Formula I can be prepared as a pharmaceutically acceptable acid addition salt by reacting the free base form of the compound with a pharmaceutically acceptable inorganic or organic acid. Alternatively, a pharmaceutically acceptable base addition salt of a compound of Formula I can be prepared by reacting the free acid form of the compound with a pharmaceutically acceptable inorganic or organic base. Inorganic and organic acids and bases suitable for the preparation of the pharmaceutically acceptable salts of compounds of Formula I are set forth in the definitions section of this application. Alternatively, the salt forms of the compounds of Formula I can be prepared using salts of the starting materials or intermediates.

The free acid or free base forms of the compounds of Formula I can be prepared from the corresponding base addition salt or acid addition salt form. For example, a compound of Formula I in an acid addition salt form may be converted to the corresponding free base by treating with a suitable base (e.g., ammonium hydroxide solution, sodium hydroxide, or the like). A compound of Formula I in a base addition salt form can be converted to the corresponding free acid by treating with a suitable acid (e.g., hydrochloric acid, or the like).

The *N*-oxides of compounds of Formula I can be prepared by methods known to those of ordinary skill in the art. For example, *N*-oxides can be prepared by treating an unoxidized form of the compound of Formula I with an oxidizing agent (e.g., trifluoroperacetic acid, permaleic acid, perbenzoic acid, peracetic acid, *meta*-chloroperoxybenzoic acid, or the like) in a suitable inert organic solvent (e.g., a halogenated hydrocarbon such as methylene chloride) at approximately 0°C. Alternatively, the *N*-oxides of the compounds of Formula I can be prepared from the *N*-oxide of an appropriate starting material.

Compounds of Formula I in unoxidized form can be prepared from *N*-oxides of compounds of Formula I by treating with a reducing agent (e.g. sulfur, sulfur dioxide, triphenyl phosphine, lithium borohydride, sodium borohydride, phosphorus trichloride, tribromide, or the like) in a suitable organic solvent (e.g., acetonitrile, ethanol, aqueous dioxane, or the like) at 0 to 80°C.

Prodrug derivatives of the compounds of Formula I can be made by means known to

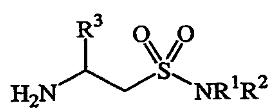
those of ordinary skill in the art (e.g., for further details see Saulnier *et al.* (1994), *Bioorganic and Medicinal Chemistry Letters*. No. 16, Vol. 4, pp. 1985-1990). For example, appropriate drugs can be prepared by reacting a non-derivatized compound of Formula I with a suitable carbamylating agent (e.g., 1,1-acyloxyalkylcarbonochloridate, *para*-nitrophenyl carbonate, or the like).

Protected derivatives of the compounds of Formula I can be made by means known to those of ordinary skill in the art. A detailed description of the techniques applicable to the creation of protective groups and their removal can be found in T.W. Greene and P.G.M. Wuts, *Protective Groups in Organic Synthesis*, John Wiley & Sons, Inc. (3rd Edition) 1999.

Compounds of Formula I can be prepared as their individual stereoisomers by reacting a racemic mixture of the compound with an optically active resolving agent to form a pair of diastereoisomeric compounds, separating the diastereomers and recovering the optically pure enantiomer. While resolution of enantiomers can be carried out using covalent diastereomeric derivatives of compounds of Formula I, dissociable complexes are preferred (e.g., crystalline diastereoisomeric salts). Diastereomers have distinct physical properties (e.g., melting points, boiling points, solubilities, reactivity, and the like) and can be readily separated by taking advantage of these dissimilarities. The diastereomers can be separated by chromatography or, preferably, by separation/resolution techniques based upon differences in solubility. The optically pure enantiomer is then recovered, along with the resolving agent, by any practical means that would not result in racemization. A more detailed description of the techniques applicable to the resolution of stereoisomers of compounds from their racemic mixture can be found in Jean Jacques Andre Collet, Samuel H. Wilen, Enantiomers, Racemates and Resolutions, John Wiley & Sons, Inc. (1981).

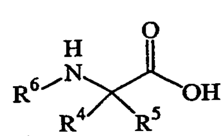
In Summary, the compounds of Formula I are made by a process which comprises:

(A) reacting a compound of formula 4:



4

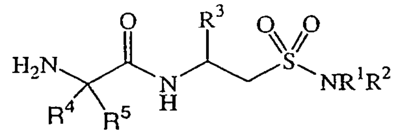
with a compound of formula 5:



5

in which R^1, R^2, R^3, R^4, R^5 and R^6 are as defined in the Summary of the Invention; or

(B) reacting a compound of formula 7:



7

with an acid compound of formula R^6OH or an acid derivative thereof, wherein R^1, R^2, R^3, R^4, R^5 and R^6 are defined in the Summary of the Invention; and

(C) optionally converting a compound of Formula I into a pharmaceutically acceptable salt;

(D) optionally converting a salt form of a compound of Formula I to non-salt form;

(E) optionally converting an unoxidized form of a compound of Formula I into a pharmaceutically acceptable *N*-oxide;

(F) optionally converting an *N*-oxide form of a compound of Formula I its unoxidized form;

(G) optionally resolving an individual isomer of a compound of Formula I from a mixture of isomers;

(H) optionally converting a non-derivatized compound of Formula I into a pharmaceutically prodrug derivative;

(I) optionally converting a prodrug derivative of a compound of Formula I to its non-derivatized form; and

(J) optionally modifying any of the R^1, R^2, R^3, R^4, R^5 and R^6 groups.

Pharmacology and Utility

The compounds of the invention are cysteine protease inhibitors. In particular the compounds of the invention inhibit the activity of cathepsins B, L, K and/or S and, as such, are useful for treating diseases in which cathepsin B, L, K and/or S activity contributes to the pathology and/or symptomatology of the disease. For example, the compounds of the invention are useful in treating tumor invasion and metastasis, in particular as anti-angiogenic agents, rheumatoid arthritis, osteo arthritis, pneumocystis carinii, acute pancreatitis, inflammatory airway disease and bone and joint disorders. Furthermore, the compounds of the invention are useful in treating bone resorption disorders, e.g., osteoporosis. The compounds

of the invention also are useful in treating autoimmune disorders, including, but not limited to juvenile onset diabetes, multiple sclerosis, pemphigus vulgaris, Graves disease, myasthenia gravis, systemic lupus erythemotasus, rheumatoid arthritis and Hashimoto's thyroiditis. The compounds of the invention also are useful in treating allergic disorders, including, but not limited to asthma; and allogeneic immune reponses, including, but not limited to, organ transplants or tissue grafts.

The cysteine protease inhibitory activities of the compounds of the invention can be determined by methods known to those of ordinary skill in the art. Suitable *in vitro* assays for measuring protease activity and the inhibition thereof by test compounds are known. Typically, the assay measures protease-induced hydrolysis of a peptide-based substrate. Details of assays for measuring protease inhibitory activity are set forth in Examples 9, 10, 11 and 12, infra.

Administration and Pharmaceutical Compositions

In general, compounds of Formula I will be administered in therapeutically effective amounts via any of the usual and acceptable modes known in the art, either singly or in combination with another therapeutic agent. A therapeutically effective amount may vary widely depending on the severity of the disease, the age and relative health of the subject, the potency of the compound used and other factors. For example, therapeutically effective amounts of a compound of Formula I may range from 0.1 micrograms per kilogram body weight (μg/kg) per day to 10 milligram per kilogram body weight (mg/kg) per day, typically 1 μg/kg/day to 1 mg/kg/day. Therefore, a therapeutically effective amount for a 80 kg human patient may range from 10 μg/day to 100 mg/day, typically 0.1 mg/day to 10 mg/day. In general, one of ordinary skill in the art, acting in reliance upon personal knowledge and the disclosure of this Application, will be able to ascertain a therapeutically effective amount of a compound of Formula I for treating a given disease.

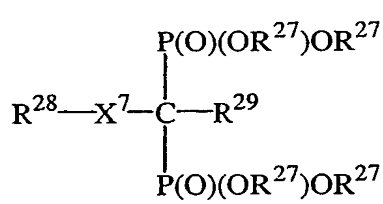
The compounds of Formula I can be administered as pharmaceutical compositions by one of the following routes: oral, systemic (e.g., transdermal, intranasal or by suppository) or parenteral (e.g., intramuscular, intravenous or subcutaneous). Compositions can take the form of tablets, pills, capsules, semisolids, powders, sustained release formulations, solutions, suspensions, elixirs, aerosols, or any other appropriate composition and are comprised of, in general, a compound of Formula I in combination with at least one pharmaceutically acceptable excipient. Acceptable excipients are non-toxic, aid administration, and do not adversely affect

the therapeutic benefit of the active ingredient. Such excipient may be any solid, liquid, semisolid or, in the case of an aerosol composition, gaseous excipient that is generally available to one of skill in the art.

Solid pharmaceutical excipients include starch, cellulose, talc, glucose, lactose, sucrose, gelatin, malt, rice, flour, chalk, silica gel, magnesium stearate, sodium stearate, glycerol monostearate, sodium chloride, dried skim milk, and the like. Liquid and semisolid excipients may be selected from water, ethanol, glycerol, propylene glycol and various oils, including those of petroleum, animal, vegetable or synthetic origin (e.g., peanut oil, soybean oil, mineral oil, sesame oil, or the like). Preferred liquid carriers, particularly for injectable solutions, include water, saline, aqueous dextrose and glycols.

The amount of a compound of Formula I in the composition may vary widely depending upon the type of formulation, size of a unit dosage, kind of excipients and other factors known to those of skill in the art of pharmaceutical sciences. In general, a composition of a compound of Formula I for treating a given disease will comprise from 0.01%w to 10%w, preferably 0.3%w to 1%w, of active ingredient with the remainder being the excipient or excipients. Preferably the pharmaceutical compositions is administered in a single unit dosage form for continuous treatment or in a single unit dosage form *ad libitum* when relief of symptoms is specifically required. Representative pharmaceutical formulations containing a compound of Formula I are described in Example 13.

The compounds of Formula I can be administered alone or in combination with other compounds of Formula I or in combination with one or more other active ingredient(s). For example, the compounds of Formula I can be administered in combination with a therapeutically active amount of a bisphosphonic acid or acid ester derivative or any pharmaceutically acceptable salt thereof. Suitable bisphosphonic acids and acid ester derivatives include compounds corresponding to the following formula:



wherein X^7 is a bond or (C_{1-7})alkylene, each R^{27} independently is hydrogen or (C_{1-30})alkyl, R^{28} and R^{29} are selected independently from a group consisting of hydrogen, halo,

optionally substituted (C_{1-30})alkyl, (C_{3-30})cycloalkyl, hetero(C_{5-30})cycloalkyl, optionally substituted (C_{6-10})aryl, hetero(C_{6-10})aryl, $NR^{30}R^{30}$, OR^{30}, SR^{30}, wherein each R^{30} independently is hydrogen, (C_{1-10})alkyl, (C_{3-10})cycloalkyl, optionally substituted (C_{6-10})aryl, provided that both R^{28} and R^{29} are not selected from hydrogen or hydroxy when X^7 is a bond; or R^{28} and R^{29} taken together form (C_{2-9})alkylene; wherein (C_{3-10})cycloalkyl includes adamantyl and the like, hetero(C_{5-10})cycloalkyl includes pyrrolidinyl and the like, (C_{6-10})aryl includes phenyl and naphthyl, and hetero(C_{6-10})aryl includes quinolyl, isoquinolyl, pyridyl, furyl, imidazolyl, imidazopyridyl and the like.

Instances wherein R^{28} and/or R^{29} are substituted (C_{1-30})alkyl may include, but are not limited to, (C_{1-30})alkyl substituted by hetero(C_{5-10})cycloalkyl, (C_{6-10})aryl, hetero(C_{6-10})aryl, $NR^{31}R^{31}$, OR^{31} and SR^{31}, wherein each R^{31} is independently hydrogen or (C_{1-10})alkyl; wherein hetero(C_{5-10})cycloalkyl includes pyrrolidinyl and the like, (C_{6-10})aryl includes phenyl and naphthyl, and hetero(C_{6-10})aryl includes quinolyl, isoquinolyl, pyridyl, furyl, imidazolyl, imidazopyridyl and the like. Suitable optionally substituted aryl groups include, but are not limited to, halo-substituted phenyl.

A non-limiting class of bisphosphonic acids and acid ester derivatives thereof suitable for administration in combination with compounds of Formula I include those in which R^{28} is selected from the group consisting of hydrogen, hydroxy or halo, and R^{29} is selected from the group consisting of optionally substituted (C_{1-30})alkyl, halo and SR^{30}, wherein R^{30} is (C_{1-10})alkyl or phenyl.

A non-limiting subclass of bisphosphonic acids and acid ester derivatives thereof suitable for administration in combination with compounds of Formula I include those in which R^{28} is selected from the group consisting of hydrogen, hydroxy and chloro and R^{29} is selected from the group consisting of optionally substituted (C_{1-30})alkyl, chloro and chlorophenylthio.

A non-limiting example of a bisphosphonic acid suitable for administration in combination with compounds of Formula I include that in which X^7 is a bond, each R^{27} is hydrogen, R^{28} is hydroxy and R^{29} is 3-aminopropyl, namely 4-amino-1-hydroxybutylidene-1,1-bisphosphonic acid (aka alendronic acid), or the monosodium trihydrate salt thereof, namely 4-amino-1-hydroxybutylidene-1,1-bisphosphonate monosodium trihydrate (aka alendronate monosodium trihydrate), described in U.S. Patents 4,922,007, to Kieczykowski et al., issued May 1, 1990; 5,019,651, to Kieczykowski et al., issued May 28, 1991; 5,510,517, to Dauer et al., issued April 23, 1996; 5,648,491, to Dauer et al., issued July 15, 1997, all of

which patents are incorporated by reference herein in their entirety.

Further non-limiting examples of bisphosphonic acids suitable for administration in combination with compounds of Formula I include the following:

cycloheptylaminomethylene-1,1-bisphosphonic acid (aka cimadronic acid), described in U.S. Patent 4,970,335, to Isomura et al., issued November 13, 1990;

1,1-dichloromethylene-1,1-diphosphonic acid (aka clodronic acid) and the disodium salt thereof, namely clodronate disodium, described in Belgium Patent 672,205 (1966) and *J. Org. Chem 32*, 4111 (1967);

1-hydroxy-3-pyrrolidin-1-ylpropylidene-1,1-bisphosphonic acid (aka EB-1053);

1-hydroxyethylidene-1,1-diphosphonic acid (aka etidronic acid);

1-hydroxy-3-(*N*-methyl-*N*-pentylamino)propylidene-1,1-bisphosphonic acid (aka ibandronic acid), described in U.S. Patent No. 4,927,814, issued May 22, 1990;

6-amino-1-hydroxyhexylidene-1,1-bisphosphonic acid (aka neridronic acid);

3-(dimethylamino)-1-hydroxypropylidene-1,1-bisphosphonic acid (aka olpadronic acid);

3-amino-1-hydroxypropylidene-1,1-bisphosphonic acid (aka pamidronic acid);

2-pyrid-2-ylethylidene-1,1-bisphosphonic acid (aka piridronic acid), described in U.S. Patent No. 4,761,406;

1-hydroxy-2-pyrid-3-ylethylidene-1,1-bisphosphonic acid (aka risedronic acid);

4-chlorophenylthiomethylenebisphosphonic acid (aka tiludronic acid), described in U.S. Patent 4,876,248, to Breliere et al., October 24, 1989; and

1-hydroxy-2-(1*H*-imidazol-1-yl)ethylidene-1,1-bisphosphonic acid (aka zoledronic acid); all of which patents and other documents referred to above are incorporated by reference herein in their entirety.

A non-limiting subclass of bisphosphonic acids suitable for administration in combination with compounds of Formula I include those selected from the group consisting of alendronic acid, cimadronic acid, clodronic acid, tiludronic acid, etidronic acid, ibandronic acid, risedronic acid, piridronic acid, pamidronic acid, zolendronic acid, pharmaceutically acceptable salts thereof, and mixtures thereof. A further example of a bisphosphonic acid suitable for administration in combination with compounds of Formula I is alendronic acid or a pharmaceutically acceptable salt thereof, and mixtures thereof. A further non-limiting example is alendronate monosodium trihydrate.

Compounds of Formula I can be administered in combination with a therapeutically

active amount of an estrogen receptor agonist. Non-limiting examples of estrogen receptor agonists suitable for administration in combination with the compounds of Formula I include naturally occurring estrogens such as estradiol, estrone and estroil, or synthetic estrogen receptor agonists such as [6-hydroxy-2-(4-hydroxyphenyl)benzo[*b*]thien-3-yl] [4-(2-piperidin-1-ylethoxy)phenyl]methanone (aka raloxifene) and {2-[4-(1,2-diphenylbut-1-enyl)-phenoxy]ethyl}dimethylamine (aka tamoxifen). A non-limiting subclass of estrogen receptor agonists suitable for administration in combination with the compounds of Formula I include estrogen receptor partial agonists (i.e., estrogen receptor agonists with mixed agonist/antagonist properties), sometimes referred to as estrogen receptor modulators. Estrogen receptor partial agonists can exert tissue-selective estrogen agonist effects. Tamoxifen, for example, selectively exerts an estrogen agonist effect on the bone, in humans. Additional suitable estrogen receptor partial agonists are described in Tissue-Selective Actions Of Estrogen Analogs, Bone Vol. 17, No. 4, October 1995, 181S-190S. Certain 3-[4-(2-phenylindol-1-ylmethyl)phenyl]acrylamides, described in U.S. Patent 5,985,910 to Miller *et al.*, November 16, 1999; benzothiphene compounds, described in U.S. Patent 5,985,897 to Meuhl *et al.*, November 16, 1999; naphthyl compounds, described in U.S. Patent 5,952,350 to Cullinan *et al.*, September 14, 1999; substituted benzothiophene compounds, described in U.S. Patent 5,962,475 to Schmid *et al.*, October 4, 1999, are suitable estrogen receptor partial agonists for administration with the compounds of Formula I; all of which patents and other documents referred to above are incorporated by reference herein in their entirety.

More particularly a pharmaceutical composition of this invention may comprise a therapeutically effect amount of a compound of Formula I in combination with one or more active ingredient(s) selected from the group consisting of (i) a therapeutically effect amount of a bisphosphonic acid or acid ester thereof or a pharmaceutically acceptable salt thereof and (ii) a therapeutically effect amount of an estrogen receptor agonist or a pharmaceutically acceptable salt thereof; and one or more pharmaceutically acceptable excipient(s). Non-limiting examples of such bisphosphonic acids include 1,1-dichloromethylene-1,1-diphosphonic acid, 1-hydroxy-3-pyrrolidin-1-ylpropylidene-1,1-bisphosphonic acid, 1-hydroxyethylidene-1,1-diphosphonic acid, 1-hydroxy-3-(*N*-methyl-*N*-pentylamino)-propylidene-1,1-bisphosphonic acid, 6-amino-1-hydroxyhexylidene-1,1-bisphosphonic acid, 3-(dimethylamino)-1-hydroxypropylidene-1,1-bisphosphonic acid, 3-amino-1-hydroxy-propylidene-1,1-bisphosphonic acid, 2-pyrid-2-ylethylidene-1,1-bisphosphonic acid, 1-

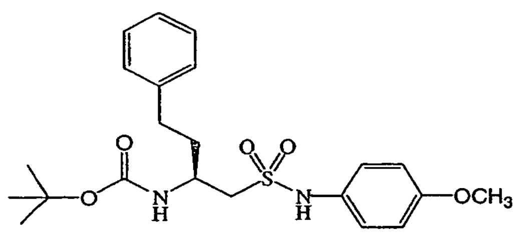
hydroxy-2-pyrid-3-ylethylidene-1,1-bisphosphonic acid, 4-chlorophenylthiomethylene-bisphosphonic acid and 1-hydroxy-2-(1*H*-imidazol-1-yl)ethylidene-1,1-bisphosphonic acid or acid ester thereof or a pharmaceutically acceptable salt thereof; particularly 1,1-dichloromethylene-1,1-diphosphonic acid or a pharmaceutically acceptable salt thereof and preferably 1,1-dichloromethylene-1,1-diphosphonate monosodium trihydrate.

EXAMPLES

The following preparations of intermediates (References) and compounds of Formula I (Examples) are given to enable those skilled in the art to more clearly understand and to practice the present invention. They should not be considered as limiting the scope of the invention, but merely as being illustrative and representative thereof.

REFERENCE 1

Synthesis of *tert*-butyl 1S-(4-methoxyphenylsulfamoylmethyl)-3-phenylpropylcarbamate, i.e., a compound of formula 3 in which PG is *tert*-butoxycarbonyl, R^1 is 4-methoxyphenyl and R^3 is 2-phenylethyl



A mixture of 1*S*-chlorosulfonylmethyl-3-phenylpropylcarbamate (0.96 g, 2.76 mmol) and 4-methoxyaniline (0.34 g, 2.76 mmol) in DCM (15 mL) was cooled to 0°C and triethylamine (0.846 mL, 6.07 mmol) was added. The mixture was stirred at room temperature for approximately 12 hours and then diluted with DCM (30 mL). The dilution was washed with 1N hydrochloric acid (30 mL), saturated aqueous sodium bicarbonate (30 mL), dried over magnesium sulfate, filtered and concentrated to dryness to provide *tert*-butyl 1S-(4-methoxyphenylsulfamoylmethyl)-3-phenylpropylcarbamate (0.60 g, 50% yield). R_f 0.4, 30% ethyl acetate/hexane. ^{1}H NMR ($CDCl_3$): 1.42 (9H, s); 1.75-1.85 (2H, m); 2.52-2.75 (2H, m); 3.08 (2H, m); 3.75 (3H, s); 4.05 (1H, m); 5.02 (1H, d, J=9 Hz); 6.75 (2H, d, J= 8 Hz) 7.07-7.28 (8H, m*).

Proceeding as in Reference 1 and using appropriate starting materials provided the

following compounds of Formula 3:

tert-butyl 1*S*-(4-hydroxyphenylsulfamoylmethyl)-3-phenylpropylcarbamate; R_f 0.45 (10% methanol/DCM);

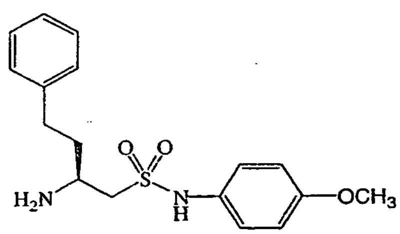
tert-butyl 1*S*-(3-acetylphenylsulfamoylmethyl)-3-phenylpropylcarbamate; R_f 0.25 (30% ethyl acetate/hexane);

benzyl 5*S*-*tert*-butoxycarbonylamino-6-(4-methoxyphenylsulfamoyl)hexylcarbamate; MS: (M+1) 536; and

benzyl 2-(4-methoxyphenylsulfamoyl)ethylcarbamate; ^{1}H NMR (chloroform-*d*): 3.20 (2H, t, J=6 Hz); 3.67 (2H, q, J=6 Hz); 3.78 (3H, s); 5..08 (2H, s); 5.39 (1H, t, J=6 Hz); 6.76 (1H, s); 6.82 (2H, d, J=9 Hz); 7.17 (2H, d, J=9 Hz); 7.32 (5H, s).

REFERENCE 2

Synthesis of 2*S*-amino-*N*-(4-methoxyphenyl)-4-phenylbutane-1-sulfonamide hydrochloride, i.e., a compound of formula 4 in which R^1 is 4-methoxyphenyl and R^3 is phenethyl



A solution comprised of crude *tert*-butyl 1-(4-methoxyphenylsulfamoylmethyl)-3-phenylpropylcarbamate (1.92 g, 4.42 mmol), prepared as in Reference 1, in DCM (10 mL) was treated with a 4M solution of hydrogen chloride in dioxane (11 mL). The mixture was stirred for 16 hours at room temperature and diluted with diethyl ether. A resulting precipitate was collected by filtration, washed several times with diethyl ether and hexane and pumped dry to provide 2*S*-amino-*N*-4-methoxyphenyl-4-phenylbutane-1-sulfonamide hydrochloride with quantitative mass recovery. ^{1}H NMR (DMSO): 2.05 (2H, m); 2.6-2.7 (2H, m); 3.4 (3H, m*); 3.72 (3H, s); 6.9 (2H, d, J=7 Hz); 7.25 (5H, m); 7.3 (2H, d, J=7 Hz); 8.5 (br. s); 10.0 (1H, s).

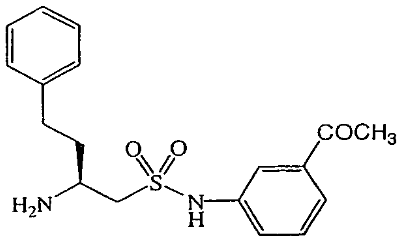
Proceeding as in Reference 2 provided the following compounds of Formula 4:

2*S*-amino-*N*-(4-hydroxyphenyl)-4-phenylbutane-1-sulfonamide hydrochloride; ^{1}H NMR (DMSO): 2.09 (2H, m); 2.72 (2H, m*); 3.68 (1H, m); 3.91-3.94 (2H, 2xdd); 7.22 (7H, m*); 7.67 (2H, d, J=7 Hz); 8.64 (2H, d, J=7 Hz); 8.7 (m*); and

benzyl 5*S*-amino-6-(4-methoxyphenylsulfamoyl)hexylcarbamate hydrochloride.

REFERENCE 3

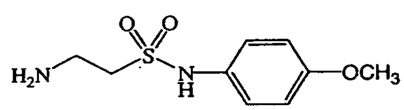
Synthesis of *N*-(3-acetylphenyl)-2*S*-amino-4-phenylbutane-1-sulfonamide *p*-toluenesulfonate, ie., a compound of formula 4 in which R^1 is 3-acetylphenyl and R^3 is 2-phenylethyl:



A solution comprised of crude *tert*-butyl 1*S*-(3-acetylphenylsulfamoylmethyl)-3-phenylpropylcarbamate, prepared as in Reference 1, in DCM (3 mL) was treated with azeotropically dried anhydrous *p*-toluenesulfonic acid (1.3 g, 6.83 mmol) in ether (3 mL). The mixture was stirred at room temperature for approximately 12 hours, diluted with diethyl ether (100 mL), washed with diethyl ether (2x30 mL) and pumped dry to provide *N*-(3-acetylphenyl)-2*S*-amino-4-phenylbutane-1-sulfonamide *p*-toluenesulfonate (1.59 g, 59% yield). ^{1}H NMR (DMSO-d^6): 1.99 (2H, m*); 2.28 (3H, s); 2.56 (3H, s*); 2.61 (2H, m*); 3.42-3.54 (3H, m*); 7.09-7.77 (13H, m*); 8.01 (2H, br. s); 10.4 (1H, s). MS (M+1, free amine): 347.

REFERENCE 4

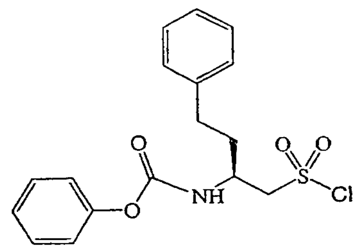
Synthesis of 2-amino-*N*-(4-methoxyphenyl)ethanesulfonamide, i.e., a compound of formula 4 in which R^1 is 4-methoxyphenyl and R^3 is hydrogen



A solution comprised of benzyl 2-(4-methoxyphenylsulfamoyl)ethylcarbamate (2.78 g, 7.63 mmol), prepared as in Reference 1, in ethanol (20 mL) and cyclohexene (20 mL) was treated with 20% palladium hydroxide (0.95 g). The mixture was heated at reflux for 2 hours, cooled, and concentrated to dryness. The solid was triturated with ether, filtered and dried to provide 2-amino-*N*-(4-methoxyphenyl)ethanesulfonamide (1.08 grams, 61% yield). ^{1}H NMR (DMSO-d^6): 2.86 (2H, t, J=6.4 Hz); 3.04 (2H, t, J=6.4 Hz); 3.72 (3H, s); 4.16 (2H, br. s); 6.87 (2H, d, J=9 Hz); 7.05 (2H, d, J=9 Hz).

REFERENCE 5

Synthesis of *tert*-butyl 1*S*-chlorosulfonylmethyl-3-phenylpropylcarbamate, i.e., a compound of formula 2 in which R^3 is phenethyl and PG is *tert*-butoxycarbonyl



A solution comprised of 2*S*-*tert*-butoxycarbonylamino-4-phenylbutyric acid (20.27 g, 72.56 mmol) in THF (100 mL) was cooled to 0 °C and then 4-methylmorpholine (7.98 mL, 72.56 mmol) and isobutyl chloroformate (9.41 mL, 72.56 mmol) were added. The mixture was allowed to stand for 10 minutes and then filtered. The filter was washed through with THF (100 mL) and the combined filtrates were added, with rapid stirring, to a solution of sodium borohydride (5.45 g, 145.1 mmol) in water (200 mL) at 0°C. The mixture was stirred for 30 minutes and then diluted with saturated aqueous sodium bicarbonate (400 mL) and ethyl acetate (200 mL). The mixture was stirred vigorously for 20 minutes, separated, and the organic phase was washed with brine (100 mL). The solution was dried over magnesium sulfate, filtered, and evaporated to dryness to provide *tert*-butyl 1*S*-hydroxymethyl-3-phenylpropylcarbamate.

The *tert*-butyl 1*S*-hydroxymethyl-3-phenylpropylcarbamate was dissolved in DCM (200 mL). The solution was cooled to 0°C and then triethylamine (27.31 mL, 195.9 mmol) was added. The mixture was stirred vigorously while methanesulfonyl chloride (13.48 mL, 174.1 mmol) was added over 5 minutes. The mixture was stirred for an additional 30 minutes and then diluted with water (200 mL). The dilution was stirred for an additional 30 minutes and then the organic phase was separated, dried over magnesium sulfate, filtered, and evaporated to dryness to provide *tert*-butyl 1*S*-methanesulfonyloxymethyl-3-phenylpropylcarbamate.

A solution of cesium thiolacetate was prepared by treating a solution of thiolacetic acid (10.36 mL, 145.1 mmol) in methanol (100 mL) with cesium carbonate (23.64 g, 72.56 mmol), concentrating the mixture and dissolving the residue in DMF (50 mL). The *tert*-butyl 1*S*-methanesulfonyloxymethyl-3-phenylpropylcarbamate was dissolved in DMF (50 mL) and added to the cesium thiolacetate solution. The mixture was stirred at room temperature for

approximately 12 hours and diluted with water (500 mL) and then ethyl acetate (300 mL). The mixture was stirred vigorously for 20 minutes and the organic phase was separated, washed with 1N hydrochloric acid (200 mL), saturated aqueous sodium bicarbonate (200 mL) and brine (200 mL), dried over a mixture of magnesium sulfate and decolorizing charcoal, filtered, and concentrated to dryness to provide *tert*-butyl 1*S*-acetylsulfanylmethyl-3-phenylpropyl)carbamate.

The *tert*-butyl 1*S*-acetylsulfanylmethyl-3-phenylpropyl)carbamate (14.73 g, 45.54 mmol) was dissolved in a 1:1 mixture of DCM:water (500 mL). The biphasic mixture was stirred rapidly and cooled to 0°C. Chlorine gas was bubbled into the solution for approximately 30 minutes (to the saturation point). The organic layer was separated, dried over magnesium sulfate, filtered, concentrated and the residue was recrystallized from DCM/hexane to provide *tert*-butyl 1*S*-chlorosulfonylmethyl-3-phenylpropylcarbamate (9.80 g, 62% yield).

Proceeding as in Reference 5 and using appropriate starting materials provided the following compounds of Formula 2:

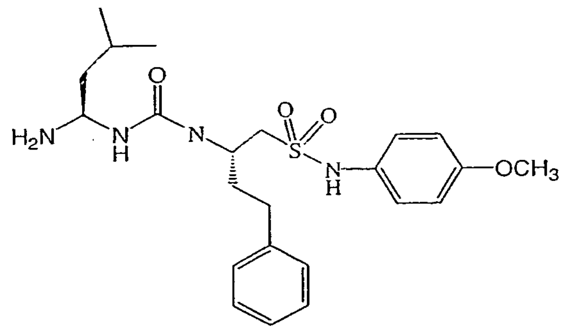
(2-chlorosulfonylethyl)-carbamic acid *tert*-butyl ester;

(5-*tert*-butoxycarbonylamino-6-chlorosulfonylhexyl)-carbamic acid benzyl ester; and

(5-amino-1-chlorosulfonylmethylpentyl)-carbamic acid *tert*-butyl ester.

REFERENCE 6

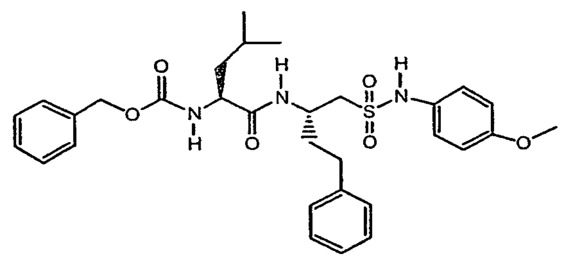
Synthesis of 2*S*-amino-*N*-[1*S*-(4-methoxyphenylsulfamoylmethyl)-3-phenylpropyl]-4-methyl-pentanamide hydrochloride, i.e., a compound of formula 6 in which R^1 is 4-methoxyphenyl, R^3 is 2-phenethyl and R^4 is 2-methylpropyl and R^5 is hydrogen



A solution of *tert*-butyl 1*S*-[1*S*-(4-methoxyphenylsulfamoylmethyl)-3-phenylpropyl-carbamoyl]-3-methylbutylcarbamate (1.1 g, 2 mmol) in dichloromethane (5 mL) was treated with a 1M solution of hydrogen chloride in diethyl ether (20 mL), with stirring, at room temperature for 5 hours and then concentrated to provide 2*S*-amino-*N*-[1*S*-(4-methoxyphenylsulfamoylmethyl)-3-phenylpropyl]-4-methylpentanamide hydrochloride (810 mg, 84% yield).

EXAMPLE 1

Synthesis of benzyl 1*S*-[1*S*-(4-methoxyphenylsulfamoylmethyl)-3-phenylpropylcarbamoyl]-3-methylbutylcarbamate (Compound 1)



A solution comprised of 2*S*-benzyloxycarbonylamino-4-methylpentanoic acid (0.25 g, 0.944 mmol) in THF (10 mL) was cooled to –10 °C and then 4-methylmorpholine (0.104 mL, 0.944 mmol) and isobutyl chloroformate (0.122 mL, 0.944 mmol) were added. The reaction mixture was allowed 5 minutes and then 2*S*-amino-*N*-(4-methoxyphenyl)-4-phenylbutane-1-sulfonamide hydrochloride (0.35 g, 0.944 mmol), prepared as in Reference 2, and 4-methylmorpholine (0.104 mL, 0.944 mmol) were added sequentially. The reaction mixture was stirred for 45 minutes and then ethyl acetate (50 mL) was added. The reaction mixture was washed with 1N hydrochloric acid, saturated sodium bicarbonate and brine (10 mL each), dried

over $MgSO_4$, filtered and concentrated. Product was purified from the residue on a silica gel column, mobile phase 30-50% ethyl acetate/hexane and crystallized from DCM/diethyl ether/hexane to provide benzyl 1*S*-[1*S*-(4-methoxyphenylsulfamoylmethyl)-3-phenylpropylcarbamoyl]-3-methylbutylcarbamate (0.172 g, 31% yield). ^1H NMR ($CDCl_3$): 0.91 (6H, 2xd*); 1.4-1.81 (4H, m*); 1.93 (1H, m); 2.55 (2H, m); 3.1-3.26 (2H, 2xdd); 3.74 (3H, s); 4.18 (1H, m); 4.22 (1H, m); 5.07 (2H, dd); 5.48 (1H, d, J=7 Hz); 6.76 (2H, d, J=9 Hz); 6.89 (1H, d); 7.04-7.28 (12H, m); 7.87 (1H, s). MS (M+1) 582.

Proceeding as in Example 1 provided the following compounds of Formula I:

benzyl 1*S*-[1*S*-(4-methoxyphenylsulfamoylmethyl)-3-phenylpropylcarbamoyl]-2-methyl-butyl-carbamate (Compound 2); ^1H NMR ($CDCl_3$): 0.85 (3H, t, J=6.5 Hz); 0.91 (3H, d, J=6.5 Hz); 1.12 (1H, m); 1.52 (1H, m); 1.8-2.05 (4H, m*); 2.55 (2H, m*); 3.18 (2H, m); 3.73 (3H, s); 4.03 (1H, m); 4.31 (1H, m); 5.09 (2H, dd); 5.31 (1H, br d); 6.76 (3H, d + m); 7.05-7.31 (12H, m); 7.62 (1H, s). MS (M+1): 582;

tert-butyl 1*S*-[1*S*-(4-methoxyphenylsulfamoylmethyl)-3-phenylpropylcarbamoyl]-3-methyl-butylcarbamate (Compound 3); ^1H NMR ($CDCl_3$): 0.85 (6H, 2xd*); 0.93 (1H, m*); 1.44 (9H, s); 1.37-1.62 (3H, m*). 2.07 (2H, m); 2.64 (2H, m); 3.62 (1H, dd, J=13.6, 3.7 Hz); 3.79 (3H, s); 3.91 (1H, dd*); 3.96 (1H, m*); 4.31 (1H, m); 4.81 (1H, m); 6.5 (1H, d, J=7.4 Hz); 7.1-7.26 (7H);

benzyl 1*S*-[1*S*-(3-acetylphenylsulfamoylmethyl)-3-phenylpropylcarbamoyl]-3-methylbutyl-carbamate (Compound 4); R_f (TLC, 20% ethyl acetate/CH_2Cl_2): 0.65; ^1H NMR ($CDCl_3$); 0.93 (6H, 2xd, J=6 Hz); 1.52 (1H, m); 1.67 (2H, m); 1.83 (1H, m); 1.98 (1H, m); 2.54-2.59 (5H, s, m*); 3.14-3.37 (2H, 2xdd); 4.11 (1H, m); 4.25 (1H, m); 5.07-5.11 (3H, s, d*); 6.59 (1H, d, J=8.4 Hz); 7.04-7.38 (13 H); 7.69 (1H, d); 7.82 (1H, s); 8.14 (1H, s). MS (M+1): 594;

N-{1*S*-[1*S*-(4-methoxyphenylsulfamoylmethyl)-3-phenylpropylcarbamoyl]-2-methylbutyl}-4-methylpiperazine-1-carboxamide (Compound 5); ^1H NMR ($CDCl_3$): 0.9 (3H, t, J=6 Hz); 1.00 (3H, d, J=6 Hz); 1.19 (1H, m); 1.56 (1H, m); 1.85 (1H, m); 2.01 (2H, m); 2.30 (3H, s); 2.42 (4H, m); 2.56 (2H, m); 3.15-3.32 (2H, 2xdd); 3.43 (4H, m); 3.77 (3H, s); 4.07 (1H, t, J=6 Hz); 4.23 (1H, m); 4.89 (1H, br d); 6.78 (2H, d); 7.00 (1H, d); 7.05-7.25 (7H, m); 8.28 (1H, br s). MS (M^+) 574; and

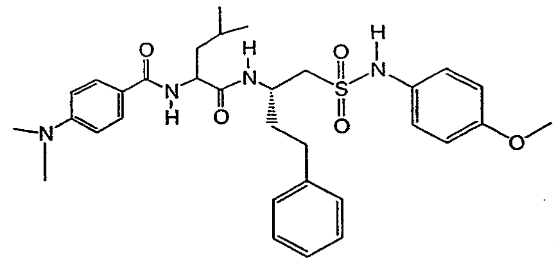
benzyl 1*S*-[2-(4-methoxyphenylsulfamoyl)ethylcarbamoyl]-2-methylbutylcarbamate (Compound 6); R_f (TLC: 50% ethyl acetate/CH_2Cl_2): 0.65; ^1H NMR ($CDCl_3$): 0.84-0.92 (6H, d, t*); 1.09 (1H, m); 1.46 (1H, m); 1.89 (1H, m); 3.22 (2H, m); 3.68 (2H, m*); 3.74 (3H, s);

4.01 (1H, t, J=6 Hz); 5.02 (2H, dd); 5.35 (1H, d, J=8 Hz); 6.85 (2H, d, J=7.5 Hz); 7.24 (2H, 7.5 Hz); 7.30 (6H, s, d*).

(2-cyclohexyl-1S-{3-phenyl-1S-[(2-phenylaminoethylsulfamoyl)-methyl]-propylcarbamoyl}ethyl)-carbamic acid *tert*-butyl ester (Compound 7);

EXAMPLE 2

Synthesis of 4-dimethylamino-*N*-{1*S*-[1*S*-(4-methoxyphenylsulfamoylmethyl)-3-phenylpropylcarbamoyl]-3-methylbutyl}benzamide (Compound 8)



A solution comprised of 2*S*-amino-*N*-(4-methoxyphenyl)-4-phenylbutane-1-sulfonamide hydrochloride (0.371 g, 1 mmol), prepared as in Reference 2, 2*S*-(4-dimethylaminobenzoylamino)-4-methylpentanoic acid (0.278 g, 1 mmol) and PyBOP (0.52 g, 1 mmol) in DMF (10 mL) was treated with triethylamine (0.418 mL, 3 mmol). The mixture was stirred at room temperature for approximately 12 hours and then diluted with ethyl acetate (30 mL), washed with 1N hydrochloric acid (10 mL) and saturated aqueous sodium bicarbonate (10 mL), dried ($MgSO_4$), filtered and concentrated to dryness. The product was crystallized twice from DCM/diethyl ether/hexane to provide 4-dimethylamino-*N*-{1*S*-[1*S*-(4-methoxyphenyl-sulfamoylmethyl)-3-phenylpropylcarbamoyl]-3-methylbutyl}benzamide (50 mg, 8.4% yield) as a diastereomeric/rotameric mixture. ^{1}H NMR ($CDCl_3$): 0.85-1.1 (6H, 2x d, t); 1.25 (1H, m); 1.5-2.2 (5H, 5x m*); 2.56 (2H, m); 3.02 (6H, s); 3.04-3.19 (2H, m*); 3.72 (3H, 2x s) 4.2-4.44 (1H, m*); 4.45, 4.67 (1H total, 2 x dd); 6.7 (4H, 2x d*); 7.06-7.24 (8H, m*); 7.69 (2H, d, J= 8.7 Hz); 7.92, 8.0 (1H total, 2x s).

Proceeding as in Example 2 provide the following compounds of Formula I:

quinoline-6-carboxylic acid (1-{1-[(4-methoxyphenylsulfamoyl)-methyl]-3-phenyl-propylcarbamoyl}-3-methylbutyl)-amide (Compound 9);

morpholine-4-carboxylic acid (2-cyclohexyl-1S-{3-phenyl-1S-[(2-phenylamino-ethylsulfamoyl)methyl]-propylcarbamoyl}-ethyl)-amide (Compound 10);

4-(2-dimethylaminothiazol-4-yl)-N-{1S-[2-(4-methoxyphenylsulfamoyl)-

ethylcarbamoyl]-3-methyl-butyl}benzamide (Compound 11);

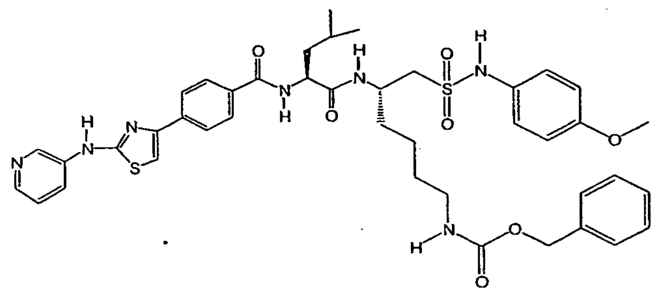
(S)-2-acetylamino-3-cyclohexyl-*N*-{1-[(4-methoxyphenylsulfamoyl)-methyl]-3-phenyl-propyl}-propionamide (Compound 12);

(*R*)-2-acetylamino-3-cyclohexyl-*N*-{1-[(4-methoxyphenylsulfamoyl)methyl]-3-phenyl-propyl}-propionamide (Compound 13);

2(*RS*)-acetylamino-3-cyclohexyl-*N*-{1-[(4-hydroxyphenylsulfamoyl)methyl]-3-phenyl-propyl}-propionamide (Compound 14).

EXAMPLE 3

Synthesis of benzyl 6-(4-methoxyphenylsulfamoyl)-5*S*-{4-methyl-2*S*-[4-(2-pyridin-3-ylaminothiazol-4-yl)-benzoylamino]pentanoylamino}hexylcarbamate (Compound 15)



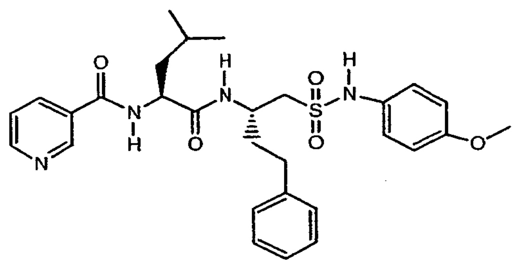
A solution comprised of benzyl 5*S*-amino-6-(4-methoxyphenylsulfamoyl)-hexylcarbamate hydrochloride (0.254 g, 0.539 mmol), prepared as in Reference 2, 4-methyl-2*S*-[4-(2-pyridin-3-ylaminothiazol-4-yl)benzoylamino]pentanoic acid hydrochloride (0.232 g, 0.539 mmol) and PyBOP (0.281 g, 0.539 mmol) in DMF (5 mL) was treated with triethylamine (0.226 mL, 1.62 mmol). The reaction mixture was stirred at room temperature for 90 minutes and then diluted with ethyl acetate (30 mL), washed with saturated aqueous sodium bicarbonate (20 mL), brine (5 mL), dried ($MgSO_4$), filtered and concentrated to dryness. The residue was triturated with 5:1 ether/dichloromethane. Solids were collected by filtration and product was purified on a short path of silica gel using 50% ethyl acetate/DCM followed by 5% methanol/DCM to provide benzyl 6-(4-methoxyphenylsulfamoyl)-5*S*-{4-methyl-2*S*-[4-(2-pyridin-3-ylaminothiazol-4-yl)benzoylamino]-pentanoylamino}hexylcarbamate. R_f (TLC: 10% methanol/DCM): 0.45. ^{1}H NMR (DMSO-d^6): 0.88 (6H, 2xd); 0.9-1.75 (9H, m*); 2.93 (2H, m); 3.09 (2H, m); 3.69 (3H, s); 4.19 (1H, m); 4.39 (1H, m); 4.99 (2H, s). 6.88 (2H, m); 7.13-7.7.45 (9H, m); 7.57 (1H, s); 7.98 (5H, m*); 8.19 (1H, d, J= 5 Hz); 8.29 (1H, d, J=7 Hz); 8.43 (1H, d, J=6 Hz); 8.86 (1H, d, J=2.4 Hz); 9.45 (1H, s); 10.6 (1H, s). MS (M+1): 828.

Proceeding as in Example 3 the following compounds of Formula I were prepared:

N-{1*S*-[1*S*-(4-methoxyphenylsulfamoylmethyl)-3-phenylpropylcarbamoyl]-3-methyl-butyl}-4-(2-pyridin-3-ylaminothiazol-4-yl)benzamide (Compound 16); ^{1}H NMR (DMSO-d^6) 0.87 (6H, 2xd); 1.23 (1H, m*); 1.5-1.86 (3H, m*); 1.99 (1H, m); 2.59 (2H, m); 3.15 (2H, m); 3.70 (3H, s); 4.24 (1H, m); 4.47 (1H, m); 6.87 (2H, d, J=9 Hz); 7.14-7.25 (7H, m); 7.43 (1H, dd); 7.58 (1H, s); 7.99 (4H, 2xd); 8.14 (1H, d); 8.19 (1H, d); 8.3 (1H, d); 8.53 (1H, d); 8.86 (1H, d); 9.48 (1H, s); 10.55 (1H, s). MS (M+1): 727.

EXAMPLE 4

Synthesis of *N*-{1*S*-[1*S*-(4-methoxyphenylsulfamoylmethyl)-3-phenylpropylcarbamoyl]-3-methylbutyl}nicotinamide (Compound 19)



A mixture comprised of 2*S*-amino-*N*-[1*S*-(4-methoxyphenylsulfamoylmethyl)-3-phenylpropyl]-4-methylpentanamide hydrochloride (110 mg, 0.227 mmol), prepared as in Reference 6, and nicotinyl chloride hydrochloride (44 mg, 0.227 mmol) in THF (2 mL) and DCM (2 mL) was treated with triethylamine (0.095 mL, 0.682 mmol). The mixture was stirred at room temperature for 3 hours and then diluted with ethyl acetate (25 mL). The dilution was washed with saturated sodium bicarbonate (5 mL), dried ($MgSO_4$), filtered and concentrated to dryness. The residue was dissolved in DCM/diethyl ether/hexane and product was crystallized to provide *N*-{1*S*-[1*S*-(4-methoxyphenylsulfamoylmethyl)-3-phenylpropylcarbamoyl]-3-methylbutyl}nicotinamide (63 mg, 50% yield). R_f (TLC, 50% ethyl acetate/DCM): 0.25. ^{1}H NMR ($CDCl_3$): 0.92-0.97 (6H, 2xd); 1.7-1.81 (4H, m*); 1.95 (1H, m); 2.54 (2H, m); 3.16 (2H, dd); 3.78 (3H, s); 4.30 (1H, m); 4.59 (1H, m); 6.74 (2H, d, J=9 Hz); 6.89 (1H, d, J=8 Hz); 7.02-7.24 (8H, m); 7.37 (1H, dd); 7.96 (1H, br s); 8.12 (1H, d, J=8 Hz); 8.71 (1H, br s); 9.06 (1H, br s). MS (M+1): 553.

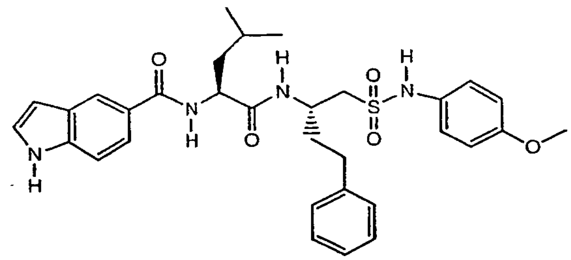
Proceeding as in Example 4 provided:

N-{1*S*-[1*S*-(4-methoxyphenylsulfamoyl-methyl)-3-phenylpropylcarbamoyl]-3-methylbutyl}-isonicotinamide (Compound 20); R_f (TLC, 20% ethyl acetate/DCM); 0.1; ^{1}H

NMR ($CDCl_3$): 0.96 (6H, 2xd); 1.65-1.89 (4H, m*); 1.98 (1H, m); 2.57 (2H, m); 3.16 (2H, 2xdd); 3.75 (3H, s); 4.30 (1H, m); 4.59 (1H, m); 6.75 (3H, d, m*); 6.85 (1H, d, J=8 Hz); 7.05-7.24 (7H, m); 7.59 (3H, m); 8.71 (2H, d); MS (M+1): 553.

EXAMPLE 5

Synthesis of *N*-{1-[1-(4-methoxyphenylsulfamoylmethyl)-3-phenylpropylcarbamoyl]-3-methylbutyl}-1*H*-indole-5-carboxamide (Compound 21)



A mixture comprised of and 2*S*-amino-*N*-[1*S*-(4-methoxyphenylsulfamoyl-methyl)-3-phenylpropyl]-4-methylpentanamide hydrochloride (0.100 g, 0.206 mmol), prepared as in Reference 6, and 5-indolecarboxylic acid (33.3 mg, 0.206 mmol) in DCM (2 mL) was treated with triethylamine (0.029 mL, 0.206 mmol) and DCC (0.206 mL of a 1.0 M DCM solution). The reaction mixture was stirred at room temperature overnight and then eluted directly through a silica gel column (0-50% ethyl acetate/CH_2Cl_2 gradient). Product was crystallized from DCM/diethyl ether/hexane to provide *N*-{1-[1-(4-methoxyphenylsulfamoylmethyl)-3-phenylpropylcarbamoyl]-3-methylbutyl}-1*H*-indole-5-carboxamide (58 mg, 48% yield). R_f (TLC, 20% ethyl acetate/CH_2Cl_2): 0.2; NMR ($CDCl_3$): 0.97-1.02 (6H, 2xd, J=6 Hz); 1.64-1.98 (5H, m*); 2.54 (2H, m); 3.02-3.19 (2H, 2xdd); 3.74 (3H, s); 4.27 (1H, m); 4.62 (1H, m); 6.48 (1H, d, J = 7 Hz); 6.61 (1H, s, t); 6.75 (2H, d, J=9 Hz); 6.94-7.27 (9H, m*); 7.41 (1H, d); 7.61 (1H, dd); 7.87 (1H, s); 8.10 (1H, s); 8.47 (1H, br s); MS (M+1): 591.

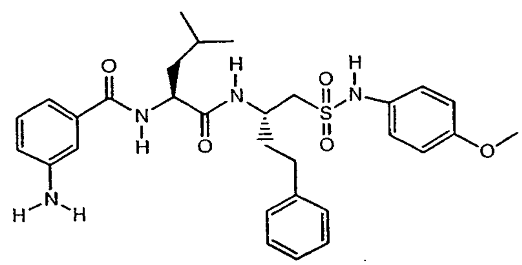
Proceeding as in Example 5 provided:

tert-Butyl 3-{1*S*-[1*S*-(4-methoxyphenyl-sulfamoylmethyl)-3-phenylpropylcarbamoyl]-3-methyl-butylcarbamoylphenyl}carbamate (Compound 22); R_f (TLC, 20% ethyl acetate/CH_2Cl_2): 0.35; ^1H NMR ($CDCl_3$): 0.93-0.99 (6H, 2xd, J=6 Hz); 1.50 (9H, s); 1.42-1.85 (4H, m*); 1.98 (1H, m); 2.58 (2H, m); 3.13 (2H, m); 3.75 (3H, s); 4.30 (1H. m); 4.60 (1H, m); 6.53 (1H, d, J=7 Hz); 6.73 (2H, d, J=9 Hz); 7.0-7.4 (11H, m*); 7.62 (1H, d, J= 7,5 Hz); 7.72 (1H, s); 7.78 (1H, s); MS (M+1): 667.

EXAMPLE 6

Synthesis of 3-amino-*N*-{1*S*-[1*S*-(4-methoxyphenylsulfamoylmethyl)-3-phenylpropylcarbamoyl]-3-methylbutyl}benzamide

(Compound 23)

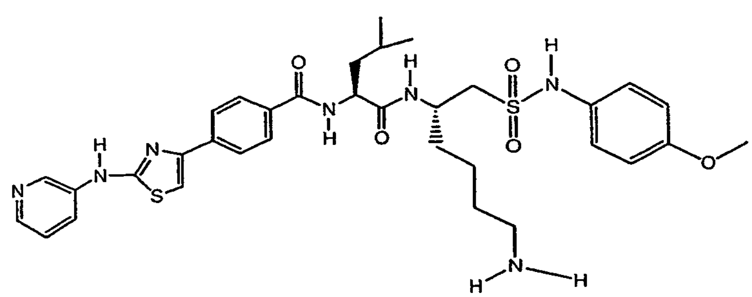


A solution comprised of *tert*-butyl 3-{1*S*-[1*S*-(4-methoxyphenylsulfamoyl-methyl)-3-phenylpropylcarbamoyl]-3-methylbutylcarbamoyl}phenylcarbamate (20 mg, 30 μmol), prepared as in Example 6, in methylene chloride (2 mL) was treated with a 4M solution of hydrochloric acid in dioxane (1 mL) at room temperature for 16 hours and then diluted with diethyl ether (100 mL) to form a precipitate. The precipitate was collected by filtration, washed with ether and dried *in vacuo* to provide 3-amino-*N*-{1*S*-[1*S*-(4-methoxyphenyl-sulfamoylmethyl)-3-phenylpropylcarbamoyl]-3-methylbutyl}benzamide (14.3 mg, 79% yield). MS (M+1, free base): 567.

EXAMPLE 7

Synthesis of *N*-{1*S*-[5-amino-1*S*-(4-methoxyphenylsulfamoylmethyl)pentylcarbamoyl]-3-methyl-butyl}-4-(2-pyridin-3-ylaminothiazol-4-yl)benzamide hydrobromide

(Compound 24)

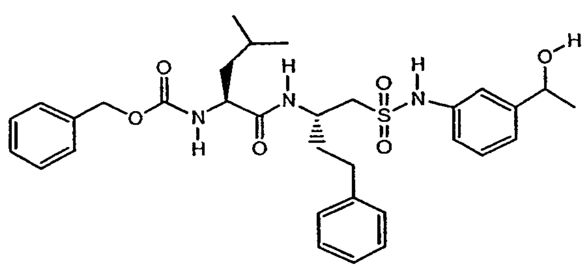


A solution of benzyl 6-(4-methoxyphenylsulfamoyl)-5*S*-{4-methyl-2*S*-[4-(2-pyridin-3-ylamino-thiazol-4-yl)benzoylamino]pentanoylamino}hexylcarbamate (0.1 g, 0.121 mmol),

prepared as in Example 3, in DCM (3 mL) was treated with 30% (0.1 g, 0.3 mL) solution of hydrogen bromide in glacial acetic acid for 3 hours. The solution was diluted with methanol/ether to form a precipitate which was isolated to provide *N*-{1*S*-[5-amino-1*S*-(4-methoxyphenylsulfamoylmethyl)pentylcarbamoyl]-3-methylbutyl}-4-(2-pyridin-3-ylaminothiazol-4-yl)benzamide hydrobromide (90 mg, 0.1 mmol). ^{1}H NMR (DMSO-d^6): 9.88 (6H, 2xd); 1.2-1.71 (9H, m); 2.72 (2H, m); 3.12 (2H, m); 3.71 (3H, s); 4.22 (1H, m); 4.43 (1H. m); 6.89 (2H, d, J=9 Hz); 7.14 (2H, d, J=9 Hz);.75 (3H, s, m*); 8.00-8.06 (7H, m); 8.53-8.66 (3H, d, d, m*); 9.47 (1H, s); 9.56 (1H, d, J=2 Hz); 11.55 (1H, s). MS (M+1, free base): 694.

EXAMPLE 8

Synthesis of benzyl 1*S*-{1*S*-[3-(1-hydroxyethyl) phenylsulfamoylmethyl]-3-phenylpropylcarbamoyl}-3-methylbutyl-carbamate (Compound 26)



A solution comprised of benzyl 1*S*-[1*S*-(3-acetylphenylsulfamoylmethyl)-3-phenylpropyl-carbamoyl]-3-methylbutylcarbamate (85 mg, 0.143 mmol), prepared as in Example 1, in THF (5 mL) was treated with sodium borohydride (10 mg, 0.266 mmol). Water (0.5 mL) was added and the mixture was stirred for 30 minutes. Saturated aqueous sodium bicarbonate (5 mL) and ethyl acetate (25 mL) were added and the mixture was stirred for 15 minutes. The organic phase was separated, dried ($MgSO_4$), filtered and concentrated to dryness to provide benzyl 1*S*-{1*S*-[3-(1-hydroxyethyl)-phenylsulfamoylmethyl]-3-phenylpropyl-carbamoyl}-3-methylbutylcarbamate (70 mg, 82% yield). R_f (TLC, 20% ethyl acetate/CH_2Cl_2): 0.2-0.3 (2 spots, corresponding to diastereomers at the hydroxyethyl group). MS(M+1): 596.

EXAMPLE 9

Cathepsin B Assay

Solutions of test compounds in varying concentrations were prepared in 10 μL of

dimethyl sulfoxide (DMSO) and then diluted into assay buffer (40 μL, comprising:*N*,*N*-bis(2-hydroxyethyl)-2-aminoethanesulfonic acid (BES), 50 mM (pH 6); polyoxyethylenesorbitan monolaurate, 0.05%; and dithiothreitol (DTT), 2.5 mM). Human cathepsin B (0.025 pMoles in 25 μL of assay buffer) was added to the dilutions. The assay solutions were mixed for 5-10 seconds on a shaker plate, covered and incubated for 30 minutes at room temperature. Z-FR-AMC (20 nMoles in 25 μL of assay buffer) was added to the assay solutions and hydrolysis was followed spectrophotometrically at (λ 460 nm) for 5 minutes. Apparent inhibition constants (K_i) were calculated from the enzyme progress curves using standard mathematical models.

Compounds of the invention were tested by the above-described assay and observed to exhibit cathepsin B inhibitory activity.

EXAMPLE 10

Cathepsin K Assay

Solutions of test compounds in varying concentrations were prepared in 10 μL of dimethyl sulfoxide (DMSO) and then diluted into assay buffer (40 μL, comprising: MES, 50 mM (pH 5.5); EDTA, 2.5 mM; and DTT, 2.5 mM). Human cathepsin K (0.0906 pMoles in 25 μL of assay buffer) was added to the dilutions. The assay solutions were mixed for 5-10 seconds on a shaker plate, covered and incubated for 30 minutes at room temperature. Z-Phe-Arg-AMC (4 nMoles in 25 μL of assay buffer) was added to the assay solutions and hydrolysis was followed spectrophotometrically at (λ 460 nm) for 5 minutes. Apparent inhibition constants (K_i) were calculated from the enzyme progress curves using standard mathematical models.

Compounds of the invention were tested by the above-described assay and observed to exhibit cathepsin K inhibitory activity.

EXAMPLE 11

Cathepsin L Assay

Solutions of test compounds in varying concentrations were prepared in 10 μL of dimethyl sulfoxide (DMSO) and then diluted into assay buffer (40 μL, comprising: MES, 50 mM (pH 5.5); EDTA, 2.5 mM; and DTT, 2.5 mM). Human cathepsin L (0.05 pMoles in 25 μL of assay buffer) was added to the dilutions. The assay solutions were mixed for 5-10 seconds

on a shaker plate, covered and incubated for 30 minutes at room temperature. Z-Phe-Arg-AMC (1 nMoles in 25 μL of assay buffer) was added to the assay solutions and hydrolysis was followed spectrophotometrically at (λ 460 nm) for 5 minutes. Apparent inhibition constants (K_i) were calculated from the enzyme progress curves using standard mathematical models.

Compounds of the invention were tested by the above-described assay and observed to exhibit cathepsin L inhibitory activity.

EXAMPLE 12

Cathepsin S Assay

Solutions of test compounds in varying concentrations were prepared in 10 μL of dimethyl sulfoxide (DMSO) and then diluted into assay buffer (40 μL, comprising: MES, 50 mM (pH 6.5); EDTA, 2.5 mM; and NaCl, 100 mM). Human cathepsin S (0.158 pMoles in 25 μL of assay buffer) was added to the dilutions. The assay solutions were mixed for 5-10 seconds on a shaker plate, covered and incubated for 30 minutes at room temperature. Z-Val-Val-Arg-AMC (9 nMoles in 25 μL of assay buffer) was added to the assay solutions and hydrolysis was followed spectrophotometrically at (λ 460 nm) for 5 minutes. Apparent inhibition constants (K_i) were calculated from the enzyme progress curves using standard mathematical models.

Compounds of the invention were tested by the above-described assay and observed to exhibit cathepsin S inhibitory activity.

EXAMPLE 13

Representative Pharmaceutical Formulations Containing a Compound of Formula I:

ORAL FORMULATION

Compound of Formula I	10-100 mg
Citric Acid Monohydrate	105 mg
Sodium Hydroxide	18 mg
Flavoring	
Water	q.s. to 100 mL

INTRAVENOUS FORMULATION

Compound of Formula I	0.1-10 mg

Dextrose Monohydrate	q.s. to make isotonic
Citric Acid Monohydrate	1.05 mg
Sodium Hydroxide	0.18 mg
Water for Injection	q.s. to 1.0 mL

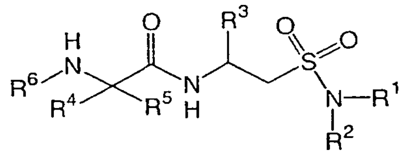
TABLET FORMULATION

Compound of Formula I	1%
Microcrystalline Cellulose	73%
Stearic Acid	25%
Colloidal Silica	1%

The foregoing invention has been described in some detail by way of illustration and example, for purposes of clarity and understanding. It will be obvious to one of skill in the art that changes and modifications may be practiced within the scope of the appended claims. Therefore, it is to be understood that the above description is intended to be illustrative and not restrictive. The scope of the invention should, therefore, be determined not with reference to the above description, but should instead be determined with reference to the following appended claims, along with the full scope of equivalents to which such claims are entitled.

We Claim:

1. A compound of Formula I:



I

in which:

R^1 and R^2 independently are $-R^8$, $-X^2OR^8$, $-X^2SR^8$, $-X^2S(O)R^8$, $-X^2S(O)_2R^8$, $-X^2C(O)R^8$, $-X^2C(OR^7)R^7R^8$, $-X^2C(O)OR^8$, $-X^2NR^7R^8$, $-X^2NR^7C(O)OR^8$, $-X^2C(O)NR^7R^8$, $-X^2S(O)_2NR^7R^8$, $-X^2NR^7C(O)NR^7R^8$ or $-X^2NR^7C(NR^7)NR^7R^8$, wherein X^2 is (C_{1-6})alkylene, R^7 is hydrogen or (C_{1-6})alkyl; R^8 is hydrogen, (C_{1-6})alkyl, (C_{3-12})cycloalkyl(C_{0-3})alkyl, hetero(C_{5-12})cycloalkyl(C_{0-3})alkyl, (C_{6-12})aryl(C_{0-3})alkyl, hetero(C_{5-12})aryl(C_{0-3})alkyl, (C_{9-12})bicycloaryl(C_{0-3})alkyl or hetero(C_{8-12})bicyclo-aryl(C_{0-3})alkyl; wherein within R^8 said cycloalkyl, heterocycloalkyl, aryl, heteroaryl, bicycloaryl or heterobicycloaryl ring may be substituted with halo, $-R^9$, $-X^3OR^9$, $-X^3SR^9$, $-X^3S(O)R^9$, $-X^3S(O)_2R^9$, $-X^3C(O)R^9$, $-X^3C(OR^9)R^9$, $-X^3C(O)OR^9$, $-X^3NR^9R^{10}$, $-X^3NR^9C(O)OR^9$, $-X^3C(O)NR^9R^{10}$, $-X^3S(O)_2NR^9R^{10}$, $-X^3NR^9C(O)NR^9R^{10}$ or $-X^3NR^9C(NR^9)NR^9R^{10}$; wherein X^3 is a bond or (C_{1-6})alkylene, R^9 is hydrogen or (C_{1-6})alkyl and R^{10} is cycloalkyl;

R^3 is $-R^{11}$, $-X^3OR^{11}$, $-X^3SR^{11}$, $-X^3S(O)R^{11}$, $-X^3S(O)_2R^{11}$, $-X^3C(O)R^{11}$, $-X^3C(O)OR^{11}$, $-X^3NR^{11}R^{12}$, $-X^3NR^{12}C(O)OR^{11}$, $-X^3C(O)NR^{11}R^{12}$, $-X^3S(O)_2NR^{11}R^{12}$, $-X^3NR^{12}C(O)NR^{11}R^{12}$ or $-X^3NR^{12}C(NR^{12})NR^{11}R^{12}$, wherein X^3 is as described above, R^{11} is hydrogen, (C_{1-6})alkyl, halo(C_{1-6})alkyl, (C_{3-12})cycloalkyl(C_{0-3})alkyl, hetero(C_{5-12})cycloalkyl-(C_{0-3})alkyl, (C_{6-12})aryl(C_{0-3})alkyl, hetero(C_{5-12})aryl(C_{0-3})alkyl, (C_{9-12})bicycloaryl(C_{0-3})alkyl or hetero(C_{8-12})bicycloaryl(C_{0-3})alkyl and R^{12} is hydrogen or (C_{1-6})alkyl, wherein any 1 to 3 annular atoms of any aromatic ring with available valences comprising R^3 are optionally independently substituted with halo, nitro, cyano, (C_{1-6})alkyl, halo-substituted(C_{1-6})alkyl, $-OR^7$, $-C(O)R^7$, $-C(O)OR^7$, $-C(O)NR^7R^7$, $-S(O)_2NR^7R^7$, $-X^2NR^7R^7$, $-X^2NR^7C(O)OR^7$, $-X^2NR^7C(O)NR^7R^7$ or $-X^2NR^7C(NR^7NR^7R^7$, wherein X^2 and $R^7$are as defined above;

R^4 is hydrogen or (C_{1-6})alkyl;

R^5 is (C_{1-6})alkyl, halo(C_{1-6})alkyl, (C_{3-12})cycloalkyl(C_{0-3})alkyl, or $-X^2S(O)R^{14}$ where X^2 is as defined above and R^{14} is (C_{3-12})cycloalkyl(C_{0-3})alkyl, hetero(C_{5-12})cycloalkyl(C_{0-3})alkyl, (C_{6-12})aryl(C_{0-3})alkyl, hetero(C_{5-12})aryl(C_{0-3})alkyl, (C_{9-12})bicycloaryl(C_{0-3})alkyl or

hetero(C_{8-12})bicycloaryl(C_{0-3})alkyl; or R^4 and R^5 together with the carbon atom to which R^4 and R^5 are attached form (C_{3-7})cycloalkylene;

R^6 is hydrogen or $-X^4X^5R^{13}$, wherein X^4 is -C(O)-, X^5 is a bond, -O- or $-NR^{12}-$, wherein R^{12} is as defined above, and R^{13} is (C_{1-6})alkyl, $-R^{14}$, $-X^3OR^{14}$, $-X^3SR^{14}$, $-X^3S(O)R^{14}$, $-X^3S(O)_2R^{14}$, $-X^3C(O)R^{14}$, $-X^3C(O)OR^{14}$, $-X^3NR^{14}R^{15}$, $-X^3NR^{15}C(O)OR^{14}$, $-X^3C(O)NR^{14}R^{15}$, $-X^3S(O)_2NR^{14}R^{15}$, $-X^3NR^{15}C(O)NR^{14}R^{15}$ or $-X^3NR^{15}C(NR^{15})NR^{14}R^{15}$, wherein X^3 is as defined above; R^{14} is (C_{3-12})cycloalkyl(C_{0-3})alkyl, hetero(C_{5-12})cycloalkyl(C_{0-3})alkyl, (C_{6-12})aryl(C_{0-3})alkyl, hetero(C_{5-12})aryl(C_{0-3})alkyl, (C_{9-12})bicycloaryl(C_{0-3})alkyl or hetero(C_{8-12})bicycloaryl(C_{0-3})alkyl; R^{15} is hydrogen or (C_{1-6})alkyl; and within R^{14} said cycloalkyl, heterocycloalkyl, aryl, heteroaryl, bicycloaryl or heterobicycloaryl ring may be substituted with $-OCF_3$, $-CF_3$, -OH, halo, $-R^{16}$, $-X^3OR^{16}$, $-X^3OR^{15}$, $-X^3C(O)R^{15}$, $-X^3SR^{16}$, $-X^3S(O)R^{16}$, $-R^{15}$, $-X^3S(O)_2R^{16}$, $-X^3C(O)R^{16}$, $-X^3C(O)OR^{15}$, $-X^3NR^{15}R^{15}$, $-X^3NR^{15}C(O)OR^{15}$, $-X^3C(O)NR^{15}R^{16}$, $-X^3S(O)_2NR^{15}R^{16}$, $-X^3NR^{15}C(O)NR^{15}R^{15}$ or $-X^3NR^{15}C(NR^{15})NR^{15}R^{16}$, wherein X^3 and R^{15} are as defined above and R^{16} is (C_{3-12})cycloalkyl(C_{0-3})alkyl, hetero(C_{5-12})cycloalkyl(C_{0-3})alkyl, (C_{6-12})aryl(C_{0-3})alkyl, hetero(C_{5-12})aryl(C_{0-3})alkyl, (C_{9-12})bicycloaryl(C_{0-3})alkyl or hetero(C_{8-12})bicycloaryl-(C_{0-3})alkyl and within R^{16} said cycloalkyl, heterocycloalkyl, aryl, heteroaryl, bicycloaryl or heterobicycloaryl ring may be substituted with $-R^{15}$, $-R^{17}$, $-X^3OR^{17}$, $-X^3SR^{17}$, $-X^3S(O)R^{17}$, $-X^3S(O)_2R^{17}$, $-X^3C(O)R^{17}$, $-X^3C(O)OR^{17}$, $-X^3NR^{15}R^{17}$, $-X^3NR^{15}R^{15}$, $-X^3NR^{15}C(O)OR^{17}$, $-X^3C(O)NR^{15}R^{17}$, $-X^3S(O)_2NR^{15}R^{17}$, $-X^3NR^{15}C(O)NR^{15}R^{17}$ or $-X^3NR^{15}C(NR^{15})NR^{15}R^{17}$, wherein X^3 and R^{15} are as defined above and R^{17} is (C_{3-12})cycloalkyl(C_{0-3})alkyl, hetero(C_{5-12})cycloalkyl(C_{0-3})alkyl, (C_{6-12})aryl(C_{0-3})alkyl, hetero(C_{5-12})aryl(C_{0-3})alkyl, (C_{9-12})bicycloaryl(C_{0-3})alkyl or hetero(C_{8-12})bicycloaryl(C_{0-3})alkyl and within R^{17} said cycloalkyl, heterocycloalkyl, aryl, heteroaryl, bicycloaryl or heterobicycloaryl ring may be substituted with $-R^{18}$, $-X^3OR^{18}$, $-X^3SR^{18}$, $-X^3S(O)R^{18}$, $-X^3S(O)_2R^{18}$, $-X^3C(O)R^{18}$, $-X^3C(O)OR^{18}$, $-X^3NR^{15}R^{18}$, $-X^3NR^{15}C(O)OR^{18}$, $-X^3C(O)NR^{15}R^{18}$, $-X^3S(O)_2NR^{15}R^{18}$, $-X^3NR^{15}C(O)NR^{15}R^{18}$ or $-X^3NR^{15}C(NR^{15})NR^{15}R^{18}$, wherein X^3 and R^{15} are as defined above and R^{18} is (C_{3-12})cycloalkyl(C_{0-3})alkyl, hetero(C_{5-12})cycloalkyl(C_{0-3})alkyl, (C_{6-12})aryl(C_{0-3})alkyl, hetero(C_{5-12})aryl(C_{0-3})alkyl, (C_{9-12})bicycloaryl(C_{0-3})alkyl or hetero(C_{8-12})bicycloaryl(C_{0-3})alkyl; with the proviso that only one (C_{9-12})bicycloaryl(C_{0-3})alkyl or hetero(C_{8-12})bicycloaryl(C_{0-3})alkyl is present within R^6, or a pharmaceutically acceptable salt thereof.

2. The compound of claim 1 in which:

R^2 is hydrogen;

R^1 is $-R^8$, $-X^2OR^8$, $-X^2C(O)R^8$, $-X^2C(OR^7)R^7R^8$, $-X^2NR^7R^8$ or $-X^2NR^7C(O)OR^8$ wherein X^2 is (C_{1-6})alkylene; R^7 is hydrogen or (C_{1-6})alkyl; R^8 is hydrogen, (C_{1-6})alkyl, (C_{3-12})cycloalkyl(C_{0-3})alkyl, hetero(C_{5-12})cycloalkyl(C_{0-3})alkyl, (C_{6-12})aryl(C_{0-3})alkyl or hetero(C_{5-12})aryl(C_{0-3})alkyl; wherein within R^8 said cycloalkyl, heterocycloalkyl, aryl or heteroaryl ring may be substituted with halo, $-R^9$, $-X^3OR^9$, $-X^3C(O)R^9$, $-X^3C(OR^9)R^9$, $-X^3NR^9R^{10}$ or $-X^3NR^9C(O)OR^9$; wherein X^3 is a bond or (C_{1-6})alkylene, R^9 is hydrogen or (C_{1-6})alkyl and R^{10} is cycloalkyl;

R^3 is $-R^{11}$, $-X^3NR^{11}R^{12}$ or $-X^3NR^{12}C(O)OR^{11}$ where R^{11} is hydrogen, (C_{1-6})alkyl, halo(C_{1-6})alkyl, (C_{3-12})cycloalkyl(C_{0-3})alkyl, hetero(C_{5-12})cycloalkyl-(C_{0-3})alkyl, (C_{6-12})aryl(C_{0-3})alkyl, hetero(C_{5-12})aryl(C_{0-3})alkyl, (C_{9-12})bicycloaryl(C_{0-3})alkyl or hetero(C_{8-12})bicycloaryl(C_{0-3})alkyl;

R^4 is hydrogen or (C_{1-6})alkyl;

R^5 is (C_{1-6})alkyl or (C_{3-12})cycloalkyl(C_{0-3})alkyl; or R^4 and R^5 together with the carbon atom to which R^4 and R^5 are attached form (C_{3-7})cycloalkylene;

R^6 is hydrogen or $-X^4X^5R^{13}$, wherein X^4 is -C(O)-, X^5 is a bond, -O- or $-NR^{12}-$, wherein R^{12} is as defined above, and R^{13} is (C_{1-6})alkyl or $-R^{14}$ wherein R^{14} is (C_{3-12})cycloalkyl(C_{0-3})alkyl, hetero(C_{5-12})cycloalkyl(C_{0-3})alkyl, (C_{6-12})aryl(C_{0-3})alkyl, hetero(C_{5-12})aryl(C_{0-3})alkyl, (C_{9-12})bicycloaryl(C_{0-3})alkyl or hetero(C_{8-12})bicycloaryl(C_{0-3})alkyl; and within R^{14} said cycloalkyl, heterocycloalkyl, aryl, heteroaryl, bicycloaryl or heterobicycloaryl ring may be substituted with $-OCF_3$, $-CF_3$, -OH, halo, $-R^{16}$, $-X^3OR^{16}$, $-X^3OR^{15}$, $-X^3C(O)R^{15}$, $-R^{15}$, $-X^3C(O)R^{16}$, $-X^3C(O)OR^{15}$, $-X^3NR^{15}R^{15}$, $-X^3NR^{15}C(O)OR^{15}$, wherein X^3 and R^{15} are as defined above and R^{16} is (C_{3-12})cycloalkyl(C_{0-3})alkyl, hetero(C_{5-12})cycloalkyl(C_{0-3})alkyl, (C_{6-12})aryl(C_{0-3})alkyl or hetero(C_{5-12})aryl(C_{0-3})alkyl, and within R^{16} said cycloalkyl, heterocycloalkyl, aryl or heteroaryl ring may be substituted with $-R^{15}$, $-R^{17}$, $-X^3NR^{15}R^{17}$, or $-X^3NR^{15}R^{15}$ wherein X^3 and R^{15} are as defined above and R^{17} is (C_{3-12})cycloalkyl(C_{0-3})alkyl, hetero(C_{5-12})cycloalkyl(C_{0-3})alkyl, (C_{6-12})aryl(C_{0-3})alkyl or hetero(C_{5-12})aryl(C_{0-3})alkyl.

3. The compound of claim 1 wherein R^1 is 4-methoxyphenyl, 3-methoxyphenyl, 2-methoxyphenyl, 4-chlorophenyl, 3-chlorophenyl, 2-chlorophenyl, 4-hydroxyphenyl, 2-acetyl-phenyl, 2-(1-hydroxyethyl)-phenyl, 2-phenylaminoethyl, pyridin-4-ylphenyl, pyridin-3-yl-phenyl, pyridin-2-ylphenyl, 1H-imidazol-2-yl, piperidin-4-yl or 1-methyl-piperidin-4-yl; and R^2 is hydrogen.

4. The compound of claim 3 in which R^3 is hydrogen, phenethyl, 4-amino-butyl, butyl or 4-benzyloxycarbonylaminobutyl.

5. The compound of claim 4 in which R^5 is isobutyl, *sec*-butyl or cyclohexylmethyl; and R^4 is hydrogen, or R^4 and R^5 together with the carbon atom to which R^4 and R^5 are attached form cyclohexyl.

6. The compound of claim 5 in which R^6 is selected from the group consisting of benzoyl, morpholin-4-ylcarbonyl, acetyl, furan-3-ylcarbonyl, 2-methoxybenzoyl, 3-methoxybenzoyl, naphthalen-2-ylcarbonyl, benzo[1,3]dioxol-5-ylcarbonyl, 3-pyridin-3-ylacryloyl, benzofuran-2-ylcarbonyl, furan-2-ylcarbonyl, *tert*-butoxycarbonyl, biphenyl-4-carbonyl, quinolin-2-ylcarbonyl, quinolin-3-ylcarbonyl, 3-acetylbenzoyl, 4-phenoxybenzoyl, 3-hydroxybenzoyl, 4-hydroxybenzoyl, pyridin-3-ylcarbonyl, 3-(*tert*-butoxycarbonylaminomethyl)benzoyl, 4-carbonylpiperazin-1-ylcarboxylic acid *tert*-butyl ester, 4-carbonylpiperazin-1-ylcarboxylic acid ethyl ester, 4-(furan-2-ylcarbonyl)piperazin-1-ylcarbonyl, pyridin-4-ylcarbonyl, 1-oxypyridin-4-ylcarbonyl, 1-oxypyridin-3-ylcarbonyl, thiophen-2-ylcarbonyl, thiophen-3-ylcarbonyl, 4-benzoylbenzoyl, 5-methylthiophen-2-ylcarbonyl, 3-chlorothiophen-2-ylcarbonyl, 3-bromothiophen-2-ylcarbonyl, 4-chlorobenzoyl, 3-flouro-4-methoxybenzoyl, 4-methoxy-benzoyl, 4-triflouromethoxybenzoyl, 3,4-difiourobenzoyl, 4-fluorobenzoyl, 3,4-dimethoxy-benzoyl, 3-methylbenzoyl, 4-bromobenzoyl, 4-triflouromethylbenzoyl, 3-benzoylbenzoyl, cyclopentanecarbonyl, benzo[b]thiophen-2-ylcarbonyl, 3-chlorobenzo[b]thiophen-2-ylcarbonyl, formamylmethyl ester, 4-methylpentanoyl, formamylisobutyl ester, formamylmonoallyl ester, formamylisopropyl ester, *N,N*-dimethylformamyl, *N*-isopropylformamyl, *N*-pyridin-4-yl-formamyl, *N*-pyridin-3-ylformamyl, 3-phenylacryloyl, 1H-indol-5-ylcarbonyl, pyridin-2-ylcarbonyl, pyrazin-2-ylcarbonyl, 3-hydroxypyridin-2-ylcarbonyl, 2-aminopyridin-3-ylcarbonyl, 2-hydroxypyridin-3-ylcarbonyl, 6-aminopyridin-3-ylcarbonyl, 6-hydroxypyridin-3-ylcarbonyl, pyridazin-4-ylcarbonyl, 3-phenoxybenzoyl, 1-oxo-1,3-dihydroisoindol-2-ylcarbonyl, 4-(4-methylpiperazin-1-yl)benzoyl, 4-morpholin-4-ylbenzoyl, 4-[2-(pyridin-3-ylamino)thiazol-4-yl]-benzoyl, 4-(2-dimethylaminothiazol-4-yl)benzoyl, quinolin-6-ylcarbonyl, 4-dimethylamino-benzoyl, 3-aminobenzoyl, 4-methylpiperazin-1-ylcarbonyl and benzylacetyl.

7. The compound of Claim 1 wherein:

R^1 is 4-methoxyphenyl, 3-acetylphenyl, 3-(1-hydroxyethyl)-phenyl, 2-(phenylamino)ethyl or 4-hydroxyphenyl;

R^2 is hydrogen;

R^3 is hydrogen, 2-phenethyl, 4-aminobutyl, or 4-benzyloxycarbonylaminobutyl;

R^4 is hydrogen;

R^5 is isobutyl, *sec*-butyl or cyclohexylmethyl; or R^4 and R^5 together with the carbon atom to which R^4 and R^5 are attached form cyclohexyl; and

R^6 is selected from the group consisting of acetyl, pyridin-3-ylcarbonyl, 3-(*tert*-butoxycarbonylamino)benzoyl, pyridin-4-ylcarbonyl, 1H-indol-5-ylcarbonyl, benzyloxycarbonyl, 3-aminobenzoyl, 4-methylpiperazin-1-ylcarbonyl, quinolin-6-ylcarbonyl, 4-[2-(pyridin-3-ylamino)thiazol-4-yl]benzoyl, 4-dimethylaminobenzoyl, morpholin-4-yl-carbonyl, 4-(2-dimethylaminothiazol-4-yl)benzoyl, *tert*-butoxycarbonyl, 4-(4-ethylpiperazin-1-yl)-benzoyl, and 4-[2-(4-methylpiperazin-1-yl)thiazol-4-yl]benzoyl.

8. The compound of claim 1 in which R^6 is selected from the group consisting of benzoyl, morpholin-4-ylcarbonyl, acetyl, furan-3-ylcarbonyl, 2-methoxybenzoyl, 3-methoxybenzoyl, naphthalen-2-ylcarbonyl, benzo[1,3]dioxol-5-ylcarbonyl, 3-pyridin-3-ylacryloyl, benzofuran-2-ylcarbonyl, furan-2-ylcarbonyl, *tert*-butoxycarbonyl, biphenyl-4-carbonyl, quinolin-2-ylcarbonyl, quinolin-3-ylcarbonyl, 3-acetylbenzoyl, 4-phenoxybenzoyl, 3-hydroxybenzoyl, 4-hydroxybenzoyl, pyridin-3-ylcarbonyl, 3-(*tert*-butoxycarbonylaminomethyl)benzoyl, 4-carbonylpiperazin-1-ylcarboxylic acid *tert*-butyl ester, 4-carbonylpiperazin-1-ylcarboxylic acid ethyl ester, 4-(furan-2-ylcarbonyl)piperazin-1-ylcarbonyl, pyridin-4-ylcarbonyl, 1-oxypyridin-4-ylcarbonyl, 1-oxypyridin-3-ylcarbonyl, thiophen-2-ylcarbonyl, thiophen-3-ylcarbonyl, 4-benzoylbenzoyl, 5-methylthiophen-2-ylcarbonyl, 3-chlorothiophen-2-ylcarbonyl, 3-bromothiophen-2-ylcarbonyl, 4-chlorobenzoyl, 3-flouro-4-methoxybenzoyl, 4-methoxy-benzoyl, 4-triflouromethoxybenzoyl, 3,4-diflourobenzoyl, 4-fluorobenzoyl, 3,4-dimethoxy-benzoyl, 3-methylbenzoyl, 4-bromobenzoyl, 4-triflouromethylbenzoyl, 3-benzoylbenzoyl, cyclopentanecarbonyl, benzo[b]thiophen-2-ylcarbonyl, 3-chlorobenzo[b]thiophen-2-ylcarbonyl, formamylmethyl ester, 4-methylpentanoyl, formamylisobutyl ester, formamylmonoallyl ester, formamylisopropyl ester, *N,N*-dimethylformamyl, *N*-isopropylformamyl, *N*-pyridin-4-yl-formamyl, *N*-pyridin-3-ylformamyl, 3-phenylacryloyl, 1H-indol-5-ylcarbonyl, pyridin-2-ylcarbonyl, pyrazin-2-ylcarbonyl, 3-hydroxypyridin-2-ylcarbonyl, 2-aminopyridin-3-ylcarbonyl, 2-hydroxypyridin-3-ylcarbonyl, 6-aminopyridin-3-ylcarbonyl, 6-hydroxypyridin-3-ylcarbonyl, pyridazin-4-ylcarbonyl, 3-phenoxybenzoyl, 1-oxo-1,3-dihydroisoindol-2-ylcarbonyl, 4-(4-methylpiperazin-1-yl)benzoyl, 4-morpholin-4-ylbenzoyl, 4-[2-(pyridin-3-ylamino)thiazol-4-yl]-benzoyl, 4-(2-dimethylaminothiazol-4-yl)benzoyl, quinolin-6-ylcarbonyl, 4-dimethylamino-benzoyl, 3-aminobenzoyl, 4-methylpiperazin-1-ylcarbonyl and benzylacetyl.

9. A compound selected from the group consisting of:

benzyl (1S-{1S-[(4-methoxyphenylsulfamoyl)-methyl]-3-phenyl-propylcarbamoyl}-3-methyl-butyl)-carbamate;

benzyl (1S-{1S-[(4-methoxyphenylsulfamoyl)-methyl]-3-phenyl-propylcarbamoyl}-2-methyl-butyl)-carbamate;

tert-butyl (1S-{1S-[(4-methoxyphenylsulfamoyl)-methyl]-3-phenyl-propylcarbamoyl}-3-methyl-butyl)-carbamate;

benzyl (1S-{1S-[(3-acetyl-phenylsulfamoyl)-methyl]-3-phenyl-propylcarbamoyl}-3-methyl-butyl)-carbamate;

N-{1*S*-[1*S*-(4-methoxyphenylsulfamoylmethyl)-3-phenylpropylcarbamoyl]-2-methylbutyl}-4-methylpiperazine-1-carboxamide;

benzyl {1S-[2-(4-methoxyphenylsulfamoyl)-ethylcarbamoyl]-2-methyl-butyl}-carbamate;

(2-cyclohexyl-1S-{3-phenyl-1S-[(2-phenylaminoethylsulfamoyl)-methyl]-propylcarbamoyl}ethyl)-carbamic acid *tert*-butyl ester;

4-dimethylamino-N-(1S-{1S-[(4-methoxyphenylsulfamoyl)methyl]-3-phenyl-propylcarbamoyl}-3-methylbutyl)-benzamide;

quinoline-6-carboxylic acid (1S-{1S-[(4-methoxyphenylsulfamoyl)methyl]-3-phenyl-propylcarbamoyl}-3-methyl-butyl)-amide;

morpholine-4-carboxylic acid (2-cyclohexyl-1S-{3-phenyl-1S-[(2-phenylamino-ethylsulfamoyl)methyl]-propylcarbamoyl}ethyl)amide;

4-(2-dimethylaminothiazol-4-yl)-N-{1S-[2-(4-methoxyphenylsulfamoyl)-ethylcarbamoyl]-3-methyl-butyl}benzamide;

2S-acetylamino-3-cyclohexyl-N-{1-[(4-methoxyphenylsulfamoyl)-methyl]-3-phenyl-propyl}propionamide;

2R-acetylamino-3-cyclohexyl-N-{1-[(4-methoxyphenylsulfamoyl)methyl]-3-phenyl-propyl}propionamide;

2RS-acetylamino-3-cyclohexyl-N-{1-[(4-hydroxyphenylsulfamoyl)methyl]-3-phenyl-propyl}-propionamide;

benzyl [6-(4-methoxyphenylsulfamoyl)-5S-(4-methyl-2S-{4-[2-(pyridin-3-ylamino)thiazol-4-yl]-benzoylamino}pentanoylamino)hexyl]carbamate;

N-(1S-{1S-[(4-methoxyphenylsulfamoyl)methyl]-3-phenylpropylcarbamoyl}-3-methyl-

butyl)-4-[2-(pyridin-3-ylamino)thiazol-4-yl]-benzamide;

N-(1S-{1S-[(4-methoxyphenylsulfamoyl)methyl]-3-phenyl-propylcarbamoyl}-3-methyl-butyl)-nicotinamide;

N-(1S-{1S-[(4-methoxyphenylsulfamoyl)-methyl]-3-phenylpropylcarbamoyl}-3-methyl-butyl)-isonicotinamide;

N-{1-[1-(4-methoxyphenylsulfamoylmethyl)-3-phenylpropylcarbamoyl]-3-methylbutyl}-1*H*-indole-5-carboxamide;

tert-butyl [3-(1S-{1S-[(4-methoxyphenylsulfamoyl)-methyl]-3-phenylpropylcarbamoyl}-3-methyl-butylcarbamoyl)phenyl]-carbamate;

3-amino-N-(1S-{1S-[(4-methoxyphenylsulfamoyl)-methyl]-3-phenylpropylcarbamoyl}-3-methyl-butyl)-benzamide;

N-(1S-{5-amino-1S-[(4-methoxyphenylsulfamoyl)methyl]pentylcarbamoyl}-3-methyl-butyl)-4-[2-(pyridin-3-ylamino)-thiazol-4-yl]-benzamide;

benzyl [1S-(1S-{[3-(1-hydroxyethyl)phenylsulfamoyl]methyl}-3-phenylpropyl-carbamoyl)-3-methylbutyl]-carbamate;

morpholine 4-carboxylic acid (1S-{5-amino-1S-[(4-methoxyphenylsulfamoyl)methyl]-pentylcarbamoyl}-2-phenylmethanesulfonylethyl)amide;

(5S-[2S-(morpholin-4-ylcarbonyl)amino]-3-phenylmethanesulfonylpropionylamino}-6-phenylsulfamoylhexyl)carbamic acid benzyl ester;

morpholine 4-carboxylic acid (1S-{1S-[(4-methoxyphenylsulfamoyl)methyl]-3-phenylpropylcarbamoyl}-2-phenylmethanesulfonylethyl)amide;

N-(1S-{1S-[(4-methoxy-phenylsulfamoyl)-methyl]-3-phenyl-propylcarbamoyl}-cyclohexyl)-4-[2-(4-methylpiperazin-1-yl)thiazol-4-yl]benzamide; and

N-(1S-{1S-[(4-methoxy-phenylsulfamoyl)-methyl]-3-phenyl-propylcarbamoyl}-cyclohexyl)-4-(4-propylpiperazin-1-yl)-benzamide; or

a pharmaceutically acceptable salt thereof.

10. A pharmaceutical composition comprising a therapeutically effective amount of a compound of Claim 1 in combination with one or more pharmaceutically acceptable excipient(s).

11. The composition of Claim 10 which further comprises one or more active ingredient(s) selected from the group consisting of (i) a therapeutically effective amount of a bisphosphonic acid or acid ester thereof or a pharmaceutically acceptable salt thereof and (ii) a therapeutically effective amount of an estrogen receptor agonist or a pharmaceutically acceptable salt thereof.

12. The composition of Claim 11 wherein the bisphosphonic acid is selected from the group consisting of 1,1-dichloromethylene-1,1-diphosphonic acid, 1-hydroxy-3-pyrrolidin-1-ylpropylidene-1,1-bisphosphonic acid, 1-hydroxyethylidene-1,1-diphosphonic acid, 1-hydroxy-3-(*N*-methyl-*N*-pentylamino)propylidene-1,1-bisphosphonic acid, 6-amino-1-hydroxyhexylidene-1,1-bisphosphonic acid, 3-(dimethylamino)-1-hydroxypropylidene-1,1-bisphosphonic acid, 3-amino-1-hydroxypropylidene-1,1-bisphosphonic acid, 2-pyrid-2-ylethylidene-1,1-bisphosphonic acid, 1-hydroxy-2-pyrid-3-ylethylidene-1,1-bisphosphonic acid, 4-chlorophenylthiomethylenebisphosphonic acid and 1-hydroxy-2-(1*H*-imidazol-1-yl)ethylidene-1,1-bisphosphonic acid or acid ester thereof or a pharmaceutically acceptable salt thereof.

13. The composition of Claim 11 wherein the bisphosphonic acid is 1,1-dichloromethylene-1,1-diphosphonic acid or a pharmaceutically acceptable salt thereof.

14. The composition of Claim 11 which comprises 1,1-dichloromethylene-1,1-diphosphonate monosodium trihydrate.

15. A method for treating a disease in an animal in which inhibition of a cysteine protease can prevent, inhibit or ameliorate the pathology and/or symptomatology of the disease, which method comprises administering to the animal a therapeutically effective amount of compound of Claim 1 or a pharmaceutically acceptable salt thereof.

16. The method of Claim 15 wherein the disease is osteoporosis.

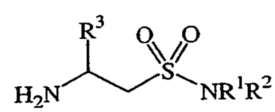
17. The method of Claim 16 wherein the animal is a human.

18. The method of Claim 17 wherein the human is a post-menopausal woman.

19. The method of Claim 18 wherein the cysteine protease activity is cathepsin K activity.

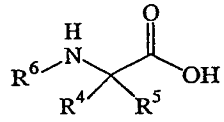
20. A process for preparing a compound of Claim1 comprising:

(A) reacting a compound of formula 4



4

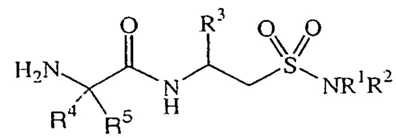
where R^1, R^2, and R^3 are as defined in Claim 1 above; with a compound of formula 5:



5

where R^6 is as defined in Claim 1 above; or

(B) reacting a compound of formula 7:



7

with an acid compound of formula R^6OH or an acid derivative thereof, wherein R^1, R^2, R^3 ,R^4, R^5 and R^6 are as defined in Claim 1 above; and

(C) optionally converting a compound of Formula I into a pharmaceutically acceptable salt;

(D) optionally converting a salt form of a compound of Formula I to non-salt form;

(E) optionally converting an unoxidized form of a compound of Formula I into a pharmaceutically acceptable *N*-oxide;

(F) optionally converting an *N*-oxide form of a compound of Formula I its unoxidized form;

(G) optionally resolving an individual isomer of a compound of Formula I from a mixture of isomers;

(H) optionally converting a non-derivatized compound of Formula I into a pharmaceutically prodrug derivative;

(I) optionally converting a prodrug derivative of a compound of Formula I to its non-derivatized form; and

(J) optionally modifying any of the R^1, R^2, R^3 ,R^4, R^5 and R^6 groups.

INTERNATIONAL SEARCH REPORT

Int ıal Application No
PCT/US 02/28505

A. CLASSIFICATION OF SUBJECT MATTER

IPC 7 C07C311/45 C07D295/215 C07D215/48 C07D277/42 C07D417/12
C07D213/82 C07D213/81 C07D209/08 C07D295/155 A61K31/18
A61K31/27 A61K31/496 A61K31/47 A61K31/5375 A61K31/426

According to International Patent Classification (IPC) or to both national classification and IPC

B. FIELDS SEARCHED

Minimum documentation searched (classification system followed by classification symbols)

IPC 7 C07C C07D

Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched

Electronic data base consulted during the international search (name of data base and, where practical, search terms used)

EPO-Internal, BEILSTEIN Data, CHEM ABS Data, WPI Data

C. DOCUMENTS CONSIDERED TO BE RELEVANT

Category °	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
A	WO 00 55144 A (MARTELLI ARNOLD J ;SAUNDERS OLIVER L (US); LINK JOHN O (US); ZIPFE) 21 September 2000 (2000-09-21) page 1, line 4 -page 2, line 6; claims; examples	1-20
A	WO 98 47523 A (CEPHALON INC) 29 October 1998 (1998-10-29) page 1, line 10 -page 2, line 32; claims; examples	1-20
A	WO 96 30353 A (ARRIS PHARM CORP) 3 October 1996 (1996-10-03) page 36, line 1 -page 38, line 28; claims; examples	1-20

-/--

[X] Further documents are listed in the continuation of box C.

[X] Patent family members are listed in annex.

° Special categories of cited documents :

"A" document defining the general state of the art which is not considered to be of particular relevance

"E" earlier document but published on or after the international filing date

"L" document which may throw doubts on priority claim(s) or which is cited to establish the publication date of another citation or other special reason (as specified)

"O" document referring to an oral disclosure, use, exhibition or other means

"P" document published prior to the international filing date but later than the priority date claimed

"T" later document published after the international filing date or priority date and not in conflict with the application but cited to understand the principle or theory underlying the invention

"X" document of particular relevance; the claimed invention cannot be considered novel or cannot be considered to involve an inventive step when the document is taken alone

"Y" document of particular relevance; the claimed invention cannot be considered to involve an inventive step when the document is combined with one or more other such documents, such combination being obvious to a person skilled in the art.

"&" document member of the same patent family

Date of the actual completion of the international search	Date of mailing of the international search report
26 November 2002	09/12/2002

Name and mailing address of the ISA	Authorized officer
European Patent Office, P.B. 5818 Patentlaan 2 NL – 2280 HV Rijswijk Tel. (+31-70) 340-2040, Tx. 31 651 epo nl, Fax: (+31-70) 340-3016	Seufert, G

INTERNATIONAL SEARCH REPORT

In....... ıal Application No
PCT/US 02/28505

A. CLASSIFICATION OF SUBJECT MATTER
IPC 7 A61K31/427 A61K31/465 A61K31/404 A61P19/02 A61P19/10
A61P35/00 A61P37/00

According to International Patent Classification (IPC) or to both national classification and IPC

B. FIELDS SEARCHED

Minimum documentation searched (classification system followed by classification symbols)

Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched

Electronic data base consulted during the international search (name of data base and, where practical, search terms used)

C. DOCUMENTS CONSIDERED TO BE RELEVANT

Category °	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
A	WO 00 48993 A (NOVARTIS ERFIND VERWALT GMBH ;ALTMANN EVA (CH); LATTMANN RENE (CH)) 24 August 2000 (2000-08-24) page 1; claims; examples -----	1-20

☐ Further documents are listed in the continuation of box C.

☒ Patent family members are listed in annex.

° Special categories of cited documents :

"A" document defining the general state of the art which is not considered to be of particular relevance
"E" earlier document but published on or after the international filing date
"L" document which may throw doubts on priority claim(s) or which is cited to establish the publication date of another citation or other special reason (as specified)
"O" document referring to an oral disclosure, use, exhibition or other means
"P" document published prior to the international filing date but later than the priority date claimed

"T" later document published after the international filing date or priority date and not in conflict with the application but cited to understand the principle or theory underlying the invention
"X" document of particular relevance; the claimed invention cannot be considered novel or cannot be considered to involve an inventive step when the document is taken alone
"Y" document of particular relevance; the claimed invention cannot be considered to involve an inventive step when the document is combined with one or more other such documents, such combination being obvious to a person skilled in the art.
"&" document member of the same patent family

Date of the actual completion of the international search	Date of mailing of the international search report
26 November 2002	

Name and mailing address of the ISA	Authorized officer
European Patent Office, P.B. 5818 Patentlaan 2 NL – 2280 HV Rijswijk Tel. (+31-70) 340-2040, Tx. 31 651 epo nl, Fax: (+31-70) 340-3016	Seufert, G

INTERNATIONAL SEARCH REPORT

International application No.
PCT/US 02/28505

Box I Observations where certain claims were found unsearchable (Continuation of item 1 of first sheet)

This International Search Report has not been established in respect of certain claims under Article 17(2)(a) for the following reasons:

1. [X] Claims Nos.:
because they relate to subject matter not required to be searched by this Authority, namely:

Although claims 15-19 are directed to a method of treatment of the human/animal body, the search has been carried out and based on the alleged effects of the compound/composition.

2. [X] Claims Nos.: –
because they relate to parts of the International Application that do not comply with the prescribed requirements to such an extent that no meaningful International Search can be carried out, specifically:

see FURTHER INFORMATION sheet PCT/ISA/210

3. [ ] Claims Nos.:
because they are dependent claims and are not drafted in accordance with the second and third sentences of Rule 6.4(a).

Box II Observations where unity of invention is lacking (Continuation of item 2 of first sheet)

This International Searching Authority found multiple inventions in this international application, as follows:

1. [ ] As all required additional search fees were timely paid by the applicant, this International Search Report covers all searchable claims.

2. [ ] As all searchable claims could be searched without effort justifying an additional fee, this Authority did not invite payment of any additional fee.

3. [ ] As only some of the required additional search fees were timely paid by the applicant, this International Search Report covers only those claims for which fees were paid, specifically claims Nos.:

4. [ ] No required additional search fees were timely paid by the applicant. Consequently, this International Search Report is restricted to the invention first mentioned in the claims; it is covered by claims Nos.:

Remark on Protest

[ ] The additional search fees were accompanied by the applicant's protest.

[ ] No protest accompanied the payment of additional search fees.

FURTHER INFORMATION CONTINUED FROM PCT/ISA/ 210

Continuation of Box I.2

The present claims refer to compounds according to the general formula I and their pharmaceutical salts. On page 9 of the description it is mentioned that "prodrug derivatives" and "protected derivatives" are meant to be included in the scope of claim 1. The terms "prodrug derivatives" and "protected derivatives" define the compounds by a reference to the desirable characteristic and/or the result to be achieved and it is not clear, which structures would be included in such a definition (Art 6 PCT). Therefore a meaningful search for compounds falling under these definitions is not possible.
Thus, the search has been carried out only for those compounds defined in the claims 1 and their pharmaceutical composition, medical use and preparation.

The applicant's attention is drawn to the fact that claims, or parts of claims, relating to inventions in respect of which no international search report has been established need not be the subject of an international preliminary examination (Rule 66.1(e) PCT). The applicant is advised that the EPO policy when acting as an International Preliminary Examining Authority is normally not to carry out a preliminary examination on matter which has not been searched. This is the case irrespective of whether or not the claims are amended following receipt of the search report or during any Chapter II procedure.

INTERNATIONAL SEARCH REPORT

Information on patent family members

International Application No
PCT/US 02/28505

Patent document cited in search report		Publication date	Patent family member(s)			Publication date
WO 0055144	A	21-09-2000	AU	3750700	A	04-10-2000
			BG	105969	A	31-05-2002
			BR	0009044	A	15-01-2002
			CN	1345314	T	17-04-2002
			CZ	20013247	A3	15-05-2002
			EP	1161422	A1	12-12-2001
			HU	0200572	A2	29-06-2002
			NO	20014483	A	01-11-2001
			SK	12872001	A3	09-05-2002
			TR	200103335	T2	22-04-2002
			WO	0055144	A1	21-09-2000
WO 9847523	A	29-10-1998	US	6348448	B1	19-02-2002
			AU	733420	B2	17-05-2001
			AU	6972098	A	13-11-1998
			EP	0975353	A1	02-02-2000
			JP	2001520674	T	30-10-2001
			NZ	500045	A	23-02-2001
			WO	9847523	A1	29-10-1998
WO 9630353	A	03-10-1996	AU	713492	B2	02-12-1999
			AU	5367496	A	16-10-1996
			CA	2216151	A1	03-10-1996
			CN	1184472	A ,B	10-06-1998
			CZ	9702981	A3	18-03-1998
			EP	0817778	A1	14-01-1998
			JP	11503417	T	26-03-1999
			NO	974403	A	17-11-1997
			NZ	305626	A	28-01-2000
			PL	322409	A1	19-01-1998
			TW	470750	B	01-01-2002
			WO	9630353	A1	03-10-1996
			US	5776718	A	07-07-1998
			ZA	9602336	A	31-07-1996
WO 0048993	A	24-08-2000	AU	2804600	A	04-09-2000
			WO	0048993	A1	24-08-2000